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TREATMENT OF HYPOPROTEINEMIA BY ORAL ADMINISTRATION OF PROTEIN HYDROLYSATE

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The importance of proteins in the blood plasma has been demonstrated by numerous investigators. Proteins are normally present in human plasma to the extent of 6.5 to 7.5 Gm. per hundred cubic centimeters with albumin and globulin fractions in the ratio of about 1.6 to 1. In addition to the proteins in the plasma there is also a large store of proteins within the body which can be called on in time of need.

Natural foods contain complex proteins which must be broken down by the digestive enzymes to amino acids and peptides before absorption from the intestines can take place. During disease the digestive processes may not be able to maintain the proteins in the plasma. The store of proteins may also be depleted by rapid loss of plasma from the raw surfaces of burns, by copious drainage of abscesses or of other inflamed cavities or by loss of plasma during prolonged operations on the gastrointestinal tract. A dog may be made hypoproteinemic by repeated plasmapheresis and kept in that state for many months.[1] Although determinations of proteins in the plasma of such an animal show low normal values, the dog is really devoid of all or most of its store of proteins and cannot mobilize proteins if the need arises. Similar depletion of proteins may take place in persons with severe burns, particularly if these are infected or are allowed to weep. Laboratory determinations made four to ten weeks after injury may show low normal values, but these do not indicate the true state of the store of proteins. If grafting operations are then attempted, acute hypoproteinemia may develop, and the grafts may not take. If patients are given adequate replacement therapy, hypoproteinemia is not likely

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1. Madden, S. C., and Whipple, G. H.: Physiol. Rev. **20**:194-217 (April) 1940.

to develop. Furthermore, there is good evidence that prolonged hypoproteinemia does not materially injure the protein-forming mechanism.[2]

Plasma proteins and the general protein store can be synthesized by the human body if it receives the proper mixture of amino acids.[1] Ten amino acids—valine, leucine, isoleucine, threonine, arginine, methionine, tryptophan, phenylalanine, histidine and lysine—are considered essential. Cystine also is important. With a mixture of amino acids or of the products synthesized from them, replacement might be accomplished by (1) direct parenteral introduction of the synthesized products in the form of hydrated or dried plasma, (2) parenteral administration of amino acids or (3) oral administration of amino acids or immediate precursors of these with a view to their absorption from the gastrointestinal tract.

The first is a satisfactory and rapid method but has certain disadvantages. Human plasma is not readily obtainable in quantities large enough for building up protein stores, notwithstanding the fact that plasma banks have been established at many centers. About 1,000 cc. of plasma is required to raise the protein content of the plasma of the average adult 1 Gm. per hundred cubic centimeters. In severe hypoproteinemia many liters of plasma may be needed. When plasma is given, absorption and synthesis are unnecessary.

The second method has been employed by Elman,[3] Farr and MacFayden,[4] Shohl and associates,[5] Whipple and associates [6] and others. Theoretically the method is good, but it presents several practical difficulties, not the least of which is the preparation of a standardized hydrolysate safe for parenteral use.

It is the third method which interested us. Amino acids are absorbed rapidly from the gastrointestinal tract. Theoretically, therefore, essential amino acids introduced into the upper jejunum should be promptly absorbed. Pure amino acids are not introduced into the intestinal tract in any considerable quantity for several reasons. They are extremely expensive and difficult to obtain in pure form. They are irritating to the upper portion of the normal small intestine if introduced in large quantities.[7] The further the breaking down of any given protein pro-

2. Madden, S. C.; Noehren, W. A.; Waraich, G. S., and Whipple, G. H.: J. Exper. Med. **69**:721-738 (May) 1939. Melnick, D., and Cowgill, G. R.: ibid. **66**:493-508 (Oct.) 1937.

3. Elman, R.: Ann. Surg. **112**:594-602 (Oct.) 1940.

4. Farr, L. E., and MacFayden, D. A.: Proc. Soc. Exper. Biol. & Med. **42**: 444-446 (Nov.) 1939.

5. Shohl, A. T.; Butler, A. M.; Blackfan, K. D., and MacLachlan, E.: J. Pediat. **15**:469-475 (Oct.) 1939.

6. Madden, S. C.; Zeldis, L. J.; Hengerer, A. D.; Miller, L. L., and Whipple, G. H.: Science **93**:330-331 (April 4) 1941.

7. Abbott, W. O.: Ann. Surg. **112**:584-593 (Oct.) 1940.

gresses, the more irritating the products become. A compromise may be effected by hydrolyzing certain proteins to the extent that the hydrolysate contains peptides in addition to amino acids. The product we have been using [8] is an enzymatic hydrolysate of proteins from beef, wheat and milk. From this mixture an adequate amount of each of the essential amino acids is obtained, including methionine, which has recently been shown to have the property of protecting the liver against chloroform and probably against similar anesthetics.[9]

The difficulties in the parenteral use of amino acids and large quantities of human plasma in smaller hospitals led us to investigate the possibility of replacing the store of proteins and proteins in the plasma by administering amino acids and somewhat larger aggregates of protein into the intestinal tract. If rapid replacement could be obtained in this manner, the method of administration would be valuable for persons with severe and extensive burns, for example, even though these persons might not have the benefit of plasma transfusions. Furthermore, if this replacement was reasonably prompt, a minimum of plasma might be employed as an initial emergency measure, to be reenforced by the oral hydrolysate.

All routine determinations of the proteins in the plasma in this study were performed by the falling drop method. We selected this method for several reasons. Hypoproteinemia is only part of the picture in the average case, and the falling drop studies give information regarding the state of hydration without which it is impossible to determine the true level of proteins. The method is accurate and compares well with the salting-out process. It does not indicate the albumin-globulin ratio and gives erroneous information under certain circumstances. The albumin-globulin ratio, however, is seldom necessary except in comparative studies. Then it can be determined by the usual Kjeldahl process. In the presence of gross hemolysis, hyperbilirubinemia, severe diabetes, gross lipemia and hypercholesteremia the falling drop method may give false results. The method depends on the close relationship between the specific gravity of the plasma and the amount of protein present. The lipemia of nephrosis, for example, may alter the specific gravity to such an extent that the falling drop calculations are confusing and unreliable. Hematocrit determination is necessary for interpretation of the plasma protein values. A hypoproteinemic patient may present an apparently normal value because of moderate hemoconcentration. Low protein values are likewise obtained at the end of pregnancy because of hydremia.

8. This preparation, known as aminoids, was supplied for this work by the Arlington Chemical Company.

9. Miller, L. L.; Ross, J. F., and Whipple, G. H.: Am. J. M. Sc. **200**:739-756 (Dec.) 1940.

To test whether the protein hydrolysate used causes a rise of protein values when introduced into the gastrointestinal tract, we employed it in treating 30 patients with hypoproteinemia due to various causes. Since the laboratory information in 3 cases was inadequate, those cases were eliminated from the calculations. Table 1 lists the types of patients treated with the hydrolysate. Six cases are briefly reported.

REPORT OF CASES

CASE 1.—A 29 year old white man was admitted on Aug. 20, 1940 in shock after sustaining extensive second and third degree burns on the arms, the back, the buttocks, the thighs, the legs and the feet and first degree burns of the abdomen. After débridement and cleansing, the burns on the trunk were sprayed with tannic acid, and those on the extremities were treated with ethylaminobenzoate ointment.

TABLE 1.—*Patients Treated by Oral Administration of the Protein Hydrolysate*

Primary Complaint	Additional Data	Patients
Carcinoma of the colon	Operated on by two stage resection	1
Carcinoma of the rectum	Operated on by one stage resection	1
Carcinoma of the rectum	Operated on by two stage resection	1
Extensive second and third degree burns		5
Thrombophlebitis of appendical vein	Infarct of the liver and lung present	1
Cholecystitis	Cholecystectomy performed and continuous suction applied	2
Appendical abscess	Continuous suction applied	1
Pyelitis of pregnancy		2
Ruptured ectopic pregnancy		1
Rectal polyps	Hemorrhage occurred repeatedly	1
Papillary cystadenoma of ovary	Operation performed	1
Strangulated hernia		1
Cirrhosis of the liver		2
Nutritional hypoproteinemia, allergy and dermatitis		2
Perforated peptic ulcer	Continuous suction applied	1
Acute glomerulonephritis		3
Lacerations of the cervix	Hemorrhage occurred repeatedly	1

Shock was controlled with elevation of the foot of the bed, heat, 10 cc. of an extract of adrenal cortex and 1,000 cc. of a 5 per cent solution of dextrose in physiologic solution of sodium chloride, given intravenously. The protein hydrolysate was given the same evening. With treatment, as shown in chart 1, his condition was good on the sixteenth day. One day later staphylococcic cellulitis developed in his right groin; this was controlled with sulfathiazole (2-[para-aminobenzenesulfonamido]-thiazole). A rapid drop of proteins in the plasma occurred but this was corrected by oral feeding of the protein hydrolysate. No plasma or whole blood was given.

CASE 2.—A 23 year old white man was injured in the same accident as the patient in case 1. He was admitted in intense pain with third degree burns of the left hand, the forearm, the arm and the shoulder, second and third degree burns of the left side of the thorax and the abdomen, second degree burns of the right hand and the forearm, and first degree burns of the penis, the scrotum, the perineum and the thighs. The burned areas were thoroughly cleaned, débrided and treated with tannic acid spray. The foot of the bed was elevated; warmth was applied, and the patient was given 2,000 cc. of a 5 per cent solution of dextrose in physiologic solution of sodium chloride and 10 cc. of an extract of adrenal

cortex intravenously. He remained in shock for many hours, but within thirty-six hours the hematocrit determination was reduced from 64 to 59 per cent. The protein hydrolysate was given orally, and the plasma proteins gradually rose, as shown in chart 2. He became ambulatory on the thirty-seventh day and later had two successful grafting operations without compromising the plasma protein values. No plasma or whole blood was given.

CASE 3.—A Negro boy 8 months old was admitted on July 6, 1940 and discharged improved to the clinic on October 3. Three weeks prior to admission his legs and feet became swollen. The swelling gradually spread over the entire body and was accompanied by a generalized maculopapular erythematous rash.

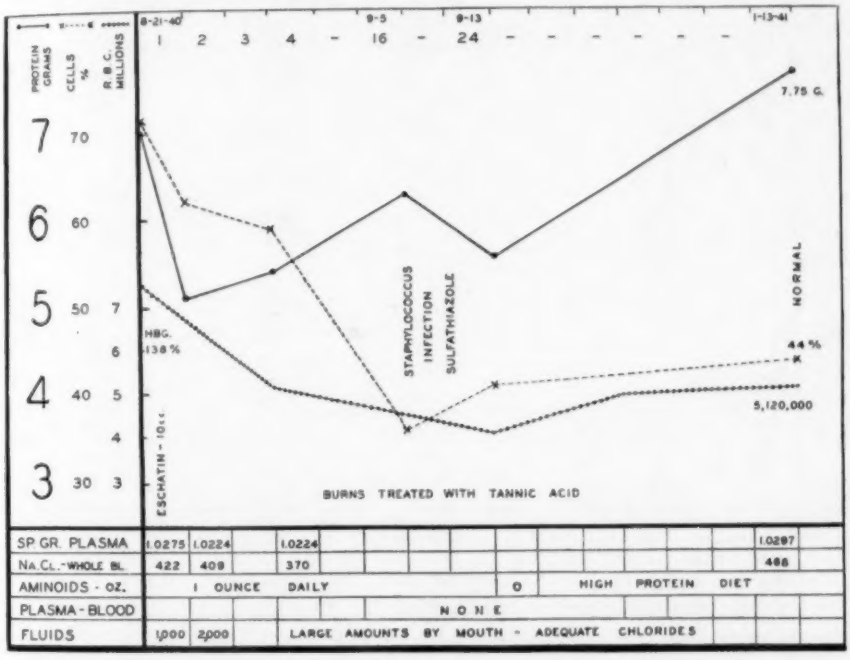
PROTEIN GRAMS
CELLS %
R.B.C. MILLIONS
8-21-40
9-5
9-13
1-13-41
1 2 3 4 - 16 - 24 - - - - - -
7.75 G.
NORMAL
44 %
5,120,000
HBG. 138 %
STAPHYLOCOCCUS INFECTION SULFATHIAZOLE
ESCHATIN - 10 cc
BURNS TREATED WITH TANNIC ACID
SP. GR. PLASMA 1.0275 1.0224 1.0224 1.0297
NA. CL. - WHOLE BL. 422 409 370 466
AMINOIDS - OZ. 1 OUNCE DAILY 0 HIGH PROTEIN DIET
PLASMA - BLOOD NONE
FLUIDS 1,000 2,000 LARGE AMOUNTS BY MOUTH - ADEQUATE CHLORIDES

Chart 1.—Treatment and course of patient in case 1, a 29 year old man.

He took breast milk twice daily but was unable to retain cow's milk. On admission he had generalized edema with pitting on pressure, in addition to the rash. The abdomen was distended and contained much fluid. Since the urine failed to show evidence of nephritis and the proteins in the plasma amounted to 2.83 Gm. per hundred cubic centimeters, a diagnosis of nutritional edema, hypoproteinemia and allergy was made. Various diets failed to raise the proteins above 2.90 Gm., and on July 22 oral administration of the hydrolysate was started. Within eight days on a dosage of 2 drachms (7.76 Gm.) daily, the child gained weight, the plasma proteins rose to 5.08 Gm. per hundred cubic centimeters and the rash lessened. Both the rash and the edema had disappeared on the fifteenth day. Ingestion of carrots brought about a return of the rash. The patient's condition was excellent up to the twenty-ninth day when administration of the hydrolysate

was discontinued. The child had also received 15 ounces (443.5 cc.) of corn syrup (Karo) and goat's milk daily. These were insufficient to maintain a stationary level of protein in the plasma. On the fifty-first day edema was again present, accompanied by a rash. The protein hydrolysate was given daily in a dose of 4 drachms (15.5 Gm.). The proteins in the plasma rose rapidly; the edema disappeared; the child gained weight, and his condition became good. Skin tests showed that he was sensitive to cow's milk, dust and several vegetables. Elimination diets indicated sensitivity to carrots and a number of other foods. Smears of his blood repeatedly showed a large percentage of eosinophils, up to 28. At the time of writing the child comes to the clinic and is in excellent condition, with plasma protein values well toward the upper limits of normal. He still takes the protein hydrolysate regularly. Data on this case are presented in chart 3.

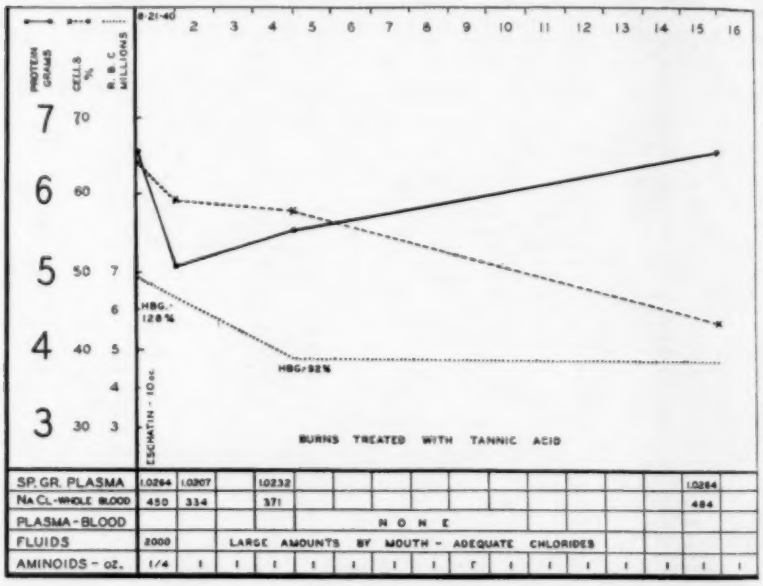
8-21-40
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
PROTEIN GRAMS
CELLS %
R.B.C. MILLIONS
7 70
6 60
5 50 7
6
4 40 5
4
3 30 3
HBG.-128%
HBG.-92%
ESCHARTIN - 10 cc.
BURNS TREATED WITH TANNIC ACID
SP. GR. PLASMA 1.0264 1.0267 1.0232 1.0284
Na Cl.-WHOLE BLOOD 450 334 371 484
PLASMA-BLOOD NONE
FLUIDS 2000 LARGE AMOUNTS BY MOUTH - ADEQUATE CHLORIDES
AMINOIDS - oz. 1/4 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1

Chart 2.—Treatment and course of patient in case 2, a 23 year old man.

CASE 4.—An acutely ill and debilitated white man 31 years old was admitted to the hospital on Nov. 19, 1940 for a plastic operation over burns sustained seven weeks before. All mucosal surfaces were dehydrated. He had large denuded granulating surfaces on his left side from third degree burns of the hand, the forearm, the arm, the thorax, the abdomen, the thigh and the leg. On the day after admission the hematocrit determination showed 46 per cent cells; the proteins in the plasma amounted to 5.27 Gm. per hundred cubic centimeters. When grafts were applied five days later he went into profound shock, from which he was retrieved with difficulty. Two days later the proteins in the plasma were down to 4.66 Gm.; after 1,000 cc. of whole blood was given, they were 5.09 Gm. After three days of dosage with 1½ ounces (44.35 cc.) of the protein hydrolysate daily, the proteins rose to 5.95 Gm. One week later he tolerated a grafting operation. He received 2,000 cc. of whole blood over a period of two months and had four

more operations. He stood these well, and his plasma proteins gradually increased to 7.38 Gm. All later grafts were successful.

CASE 5.—A Negro woman 47 years old was admitted on Nov. 14, 1940 with a history of obstipation for three days and a diagnosis of acute intestinal obstruction. At operation on November 16 the distention was found to be confined to the cecum and the ascending colon. A cecostomy was performed after an annular obstructing growth in the sigmoid colon had been located. After the operation she was given 3 ounces (88.5 cc.) of the protein hydrolysate daily by mouth, and the proteins in the plasma rose promptly (chart 4) to 7.8 Gm. per hundred cubic centimeters on December 14, when the administration of the hydrolysate was discontinued. During a stormy postoperative course atelectasis developed. On

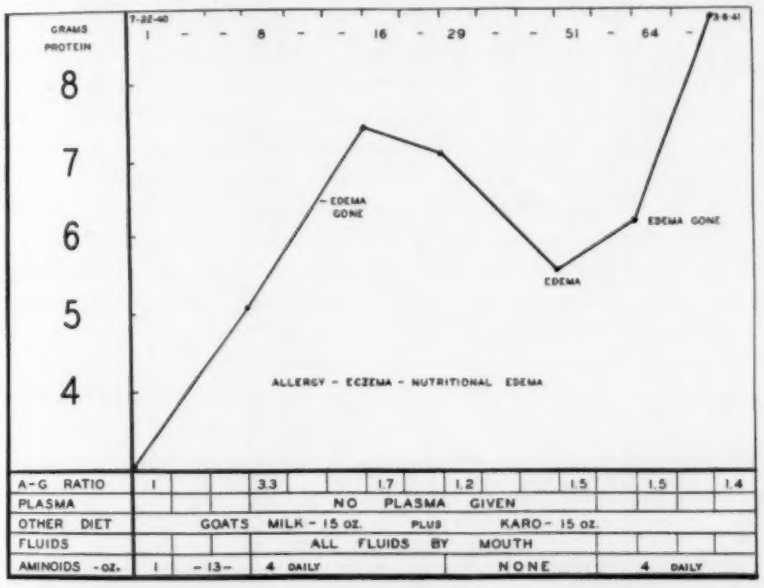
GRAMS PROTEIN
8
7
6
5
4
7-22-40
1 - - 8 - - 16 - 29 - - 51 - 64 -
EDEMA GONE
EDEMA
EDEMA GONE
ALLERGY - ECZEMA - NUTRITIONAL EDEMA
A-G RATIO 1 3.3 1.7 1.2 1.5 1.5 1.4
PLASMA NO PLASMA GIVEN
OTHER DIET GOATS MILK - 15 OZ. PLUS KARO - 15 OZ.
FLUIDS ALL FLUIDS BY MOUTH
AMINOIDS - OZ. 1 - 13 - 4 DAILY NONE 4 DAILY

Chart 3.—Treatment and course of patient in case 3, a male child 8 months old.

Jan. 16, 1941 the growth in the sigmoid colon was exteriorized by a Mikulicz operation. The proteins in the plasma dropped rapidly and four days later were 5.6 Gm. With daily administration of 3 ounces (88.5 cc.) of the protein hydrolysate the protein values became 6.8 Gm. on the day of the last operation for closure of the original cecostomy.

CASE 6.—On March 4, 1940 cholecystectomy was performed on a 51 year old white woman with cholelithiasis. Ileus developed, and the operating surgeon performed an ileostomy on March 22. Her condition was thenceforth extremely grave, and transfusions failed to maintain the proteins in the plasma within normal limits. On April 19 the value of proteins was 5.44 Gm. per hundred cubic centimeters. On April 22 the ileostomy was closed, and on April 24 a transfusion of 800 cc. of whole blood was given. Administration of the protein hydrolysate was started, ½ ounce (14.5 cc.) three times daily, because of a further drop of

the proteins to 4.93 Gm. On April 26 the value of proteins in the plasma was 4.76 Gm. and on April 27, 5.37 Gm. The proteins had increased to 6.25 Gm. on May 3. When the proteins were low, the bowel, the skin and the subcutaneous tissues were edematous. Restoration of the plasma protein levels to normal with the hydrolysate promptly eliminated the edema.

COMMENT

Many of the interesting features of the cases presented were observed in other cases of the series. Case 3 is instructive because of the profound hypoproteinemia and the inability of the patient to tolerate ordinary

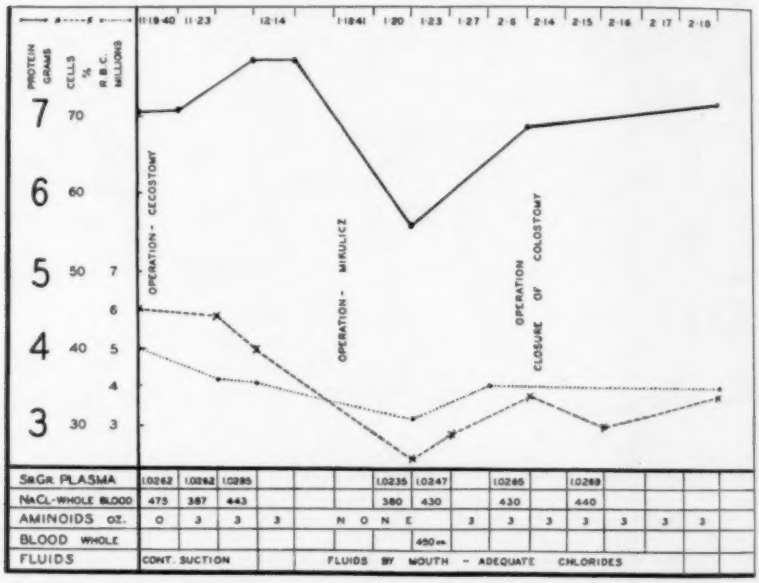

Chart 4.—Treatment and course of patient in case 5, a woman 47 years old.

forms of nourishment. With the daily administration of 2 drachms (7.5 Gm.) of the protein hydrolysate daily (about 0.75 drachm per 10 pounds [3 Gm. per 4.5 Kg.] of body weight) the proteins in the plasma were increased from 2.9 to 5.08 Gm. per hundred cubic centimeters in one week; the average daily increment was thus 0.3 Gm. At the same rate, the proteins in the plasma rose to 7.40 Gm. at the end of fifteen days. The child received corn syrup and goat's milk alone from the twenty-ninth to the fifty-first day, but the proteins fell steadily until edema reappeared a little before they reached a level of 5.6 Gm. The resumption of the protein hydrolysate feeding promptly corrected the condition for the second time, demonstrating that the rise was due to the hydrolysate. On March 6 the proteins in the plasma reached the high

level of 8.89 Gm. The child was never able to take enough of the goat's milk to maintain his weight or his plasma protein levels.

Cases 4 and 5 illustrate the danger of operating on persons whose store of proteins has become depleted and also typify two major causes of hypoproteinemia in patients who have had operations. When depletion of proteins is as severe as in case 4, the level of proteins in the plasma tends to be below normal. Unfortunately, a reduced store of proteins is not always accompanied by a low level of proteins in the plasma. The extent of depletion may not become evident until mobilization is required; then acute hypoproteinemia develops. Such a demand is made during and after an operation on the gastrointestinal tract. The protein hydrolysate should, therefore, be given orally during the preoperative and the postoperative period. During the latter period the mixture may be given through an indwelling double-barreled tube into the duodenum or the jejunum. This permits maintenance of levels of proteins and prompt healing of wounds in the intestine and the abdomen and prevents the mechanical difficulties resulting from hypoproteinemic edema. Case 5 demonstrates that it is not enough merely to raise the level of proteins in the plasma to normal. Dosage of the protein hydrolysate must be continued to build up the reserve stores; had that been done in this case the upper line on chart 4 would not dip down between the first two operations. Both cases show that the protein hydrolysate maintains satisfactory levels during and after operation. However, this was not accomplished in either case until the hydrolysate therapy was instituted.

Case 6 offers an excellent example of the pitfalls which may trap the unwary in operations on the intestine. Hypoproteinemia will develop rapidly during the period after operation. It develops mainly from three causes: the more or less prolonged malnutrition prior to operation, the loss of plasma during operation and the lack of nutriment from four to seven days after operation. The postoperative course may be complicated by drainage and continuous or interrupted suction through an indwelling tube into the duodenum or the jejunum. A patient may be able to cope with any one of these factors successfully, but he may have trouble if two are present. He surely will have trouble if all three occur, for then the usual concomitants or hypoproteinemia appear. The intestines become edematous, particularly in traumatized areas such as the suture lines; stomas from gastroenterostomy and other anastomoses become obstructed by edema; healing ceases, and a grave state of affairs comes to exist. We think that the seriousness of the situation is greatly increased if the surgeon has not properly introduced a suitable double-barreled tube well through the anastomosis into the jejunum or the duodenum as the case requires. It is then impossible to get any nutriment or fluid past the stomach. Jejunostomies performed at this time

will be worthless. The only way out is to give sufficient plasma intravenously to raise the proteins in the plasma to nearly normal levels and to be careful not to give more sodium chloride than is required. Intravenous administration of amino acids may also be indicated and may be employed if the difficulties in preparation and the dangers in use are eliminated. If the indwelling tube has been properly placed during operation, the protein hydrolysate may be introduced directly into the duodenum or the jejunum. We have successfully given the hydrolysate by this method, thereby maintaining satisfactory levels of proteins in the plasma.

To compare the results in the various cases of the series it was necessary to eliminate some of the factors which tend to make the plasma protein values incomparable. All plasma protein values were therefore corrected to conform with an ideal erythrocyte count of 4,500,000 cells and an ideal hematocrit determination of 45 per cent cells. Thus variations in blood concentration and cell counts were eliminated. Analysis of the figures obtained revealed that with few exceptions the highest daily rate of increase tended to occur during the first seven days of therapy and that the daily rate from the seventh to the twenty-sixth day seemed to decrease materially. In several cases a steady rate was maintained, and in 1 case there was actually an increase after seven days. These were exceptions. Because of these tendencies the series was first analyzed as a whole and then in two portions, the dividing line being placed at the end of the seventh day. The mean daily rise of protein in the plasma in 25 cases was 0.147 Gm., with a standard deviation of 0.1225 Gm., which shows a wide distribution about the mean value. The maximum daily rise was 0.51 Gm.; the minimum, 0.01 Gm. (chart 5). The mean daily rise during the first seven days was 0.2 Gm. with a standard deviation of 0.1228, which shows less wide distribution. The mean daily rise between the end of the seventh day and the twenty-sixth day was 0.092 Gm., less than half the rate of the first period. The standard deviation of the difference of 0.1078 between the means of the two periods was 0.0135, which indicates that the difference is probably significant. Likewise, the difference of 0.053 between the means of the entire series and of the first period had a standard deviation of 0.0117. If the 3 cases of glomerulonephritis and the 2 cases of cirrhosis of the liver are eliminated from the calculations, the results are much more striking.

Cases 1 and 2 are dealt with separately because of the complicating factors of shock and excessive hemoconcentration. The patients were treated by oral administration of the protein hydrolysate, without any plasma or whole blood. From the corrected values it will be seen that the proteins in the plasma decreased during the first seventy-two hours and afterward rose rapidly. The proteins continued to decrease for forty-eight hours after the hydrolysate therapy had been started. In

other words, it took three days for sufficient proteins to be assimilated and for the burned surfaces to be brought into sufficient control to eliminate the excessive loss of plasma. Probably this drop would not have been so prolonged if the loss of plasma had ceased promptly during the first twenty-four hours. At any rate, the administration of several thousand cubic centimeters of plasma would have prevented acute hypoproteinemia and would have greatly lessened the period of shock in each case. The protein hydrolysate taken by mouth does not appear to be adequate for alleviating shock and the accompanying acute hypoproteinemia; the oral administration of the hydrolysate should be simultaneous with an intravenous injection of plasma to reenforce the proteins and

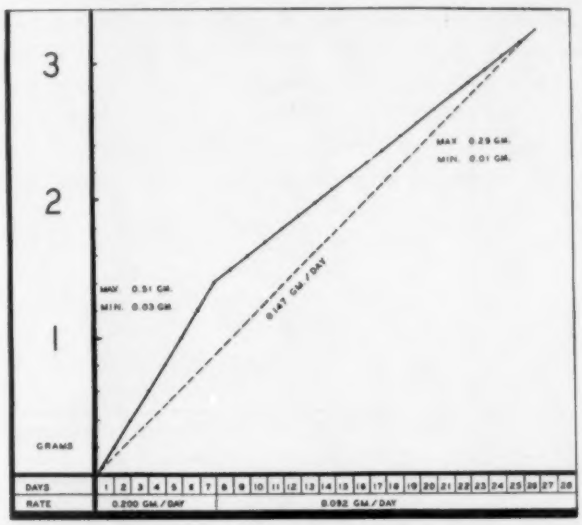

Chart 5.—Mean daily increase of proteins in the blood plasma of 25 patients treated with 1½ ounces (44.5 cc.) of the protein hydrolysate daily.

take care of the needs after the first twenty-four hours. Chart 6 depicts graphically the progress in these 2 cases.

From the oral administration of protein we have observed replenishment of the body's store of proteins, elevation of the levels of proteins in the plasma and gain in weight. One must conclude that administration of any hydrolysate of protein containing the essential amino acids and polypeptides with cystine will probably produce the same results. Furthermore, such a hydrolysate could be prepared in the hospital from readily obtainable foodstuffs. The production of a protein digest by enzymatic means is troublesome, expensive and beyond the reach of the staff of the ordinary hospital. A uniform preparation, constant in composition, readily obtainable and miscible and made up of the essential

amino acids and polypeptides would be advantageous. A diet with adequate amounts of proteins will result in replenishment of protein stores and plasma proteins. This replenishment will be much slower and will depend on the ability of the digestive tract to deal with the complex molecules of proteins. A hydrolysate is more easily dealt with.

While subcutaneous injection of amino acids and polypeptides, as recently reported,[6] appears reasonably safe, with no reactions to the preparation used, intravenous administration seems more hazardous. The authors state that an enzymatic digest of commercial casein given parenterally is as effective as whole liver given by mouth. Whether the effectiveness is greater than that of a protein hydrolysate given by mouth or through an indwelling tube cannot be stated at this time. Although

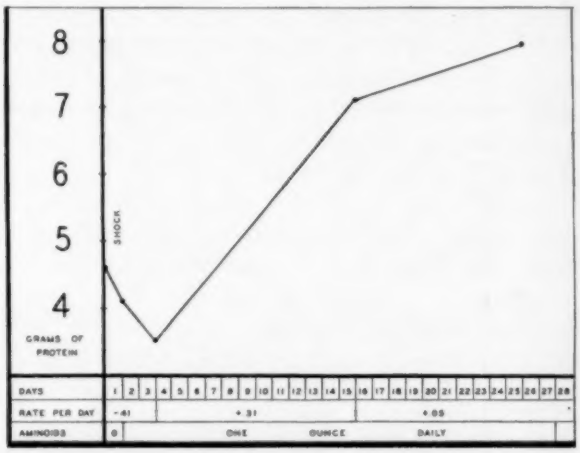

Chart 6.—Curve of average values of proteins in the plasma of patients in cases 1 and 2 after correction.

large amounts of a hydrolysate may be irritating, it is possible to give a 25 per cent solution in physiologic solution of sodium chloride or water as a slow continuous drip through an indwelling tube. Thus large amounts may be given in twenty-four hours. We have not made a sufficient study of this method to state the mean increase of plasma protein following employment of this method. The continuous drip administration is simple and requires no more than the ordinary set for administering fluids intravenously. There should be a drip chamber in the line for adjustment of the rate of flow. The 25 per cent solution of the hydrolysate is poured into the flask and the drip adjusted to a flow of about 80 drops per minute. This flow is satisfactory, and only occasionally is it necessary to flush the tube with physiologic solution of sodium chloride or water.

SUMMARY

Methods of replacement or restoration of the proteins in the plasma and the body's general store of proteins are discussed with special reference to oral feedings of a protein hydrolysate. A hydrolysate of proteins from beef, milk and wheat was employed in 30 cases for feeding by mouth or through an indwelling tube. It produced satisfactory replacement of proteins in the plasma and correction of the various anomalies which accompany hypoproteinemia. The speed of replacement was rapid but not fast enough for the treatment of shock and immediate hypoproteinemia. The hydrolysate is valuable as an adjunct to intravenously administered plasma.

Six illustrative cases are described.

The preoperative and postoperative use of such a protein hydrolysate in gastrointestinal surgical procedures is important to correct hypoproteinemia before operation and to prevent its occurrence after operation.

The protein hydrolysate, given by an indwelling tube in the duodenum or the jejunum, was well tolerated. Continuous drip feedings of a 25 per cent solution of the hydrolysate were employed. The method is described.

REGIONAL LYMPHATIC METASTASES OF CARCINOMA OF THE STOMACH

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AND

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ANN ARBOR, MICH.

The low incidence of five year cures after partial gastric resection for carcinoma of the stomach is discouraging. However, it is easily explained by the insidiousness of the disease in its early stages; by the time the symptoms become sufficiently alarming to make the patient seek medical aid, the condition is often inoperable. The elimination of certain factors to be discussed later should increase the number of five year cures.

This study, similar to one we made of the regional lymphatic metastases of carcinoma of the rectum [1] and colon,[2] is based on the dissection and examination of all the regional lymph nodes in 53 cases of carcinoma of the stomach. Fifty-one of the patients had previous partial to subtotal gastric resection, and 2 came to autopsy. The lymph nodes were dissected from each specimen after they had been visualized (fig. 1) by clearing by the Gilchrist and David modification of the Spalteholtz method.[3] Each node was examined individually and the results charted on diagrammatic drawings. The presence or absence of metastases in regional lymph nodes was then correlated with (1) the age of the patient, (2) the duration of symptoms, (3) the location of the neoplasm within the stomach, (4) the size, (5) the gross type of neoplasm, (6) the depth of infiltration, (7) the degree of cellular dif-

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From the Departments of Surgery and Pathology, University of Michigan.

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1. Coller, F. A.; Kay, E. B., and McIntyre, R. S.: Regional Lymphatic Metastases of Carcinoma of the Rectum, Surgery **8**:294 (Aug.) 1940.

2. Coller, F. A.; Kay, E. B., and McIntyre, R. S.: Regional Lymphatic Metastases of Carcinoma of the Colon, Ann. Surg. **114**:56 (July) 1941.

3. Gilchrist, R. K., and David, V. C.: Lymphatic Spread of Carcinoma of the Rectum, Ann. Surg. **108**:621, 1938.

ferentiation and (8) the microscopic type. Regional lymph nodes were thus isolated which go unnoticed by the usual method of dissection. Many large nodes were inflammatory, and many small impalpable nodes contained neoplasm. Unless a lymph node was definitely replaced by carcinoma, it was impossible to determine without microscopic section whether it was involved. Operative procedure should not be minimized because of the absence of palpable lymph nodes.

As a result of this special method of investigation, metastases in regional lymph nodes were observed in 40 of the 53 specimens (75.5 per cent). An average of 30.2 lymph nodes per specimen were isolated. There were 32.8 nodes isolated per specimen in the group having positive regional involvement, compared with 22.4 nodes per specimen

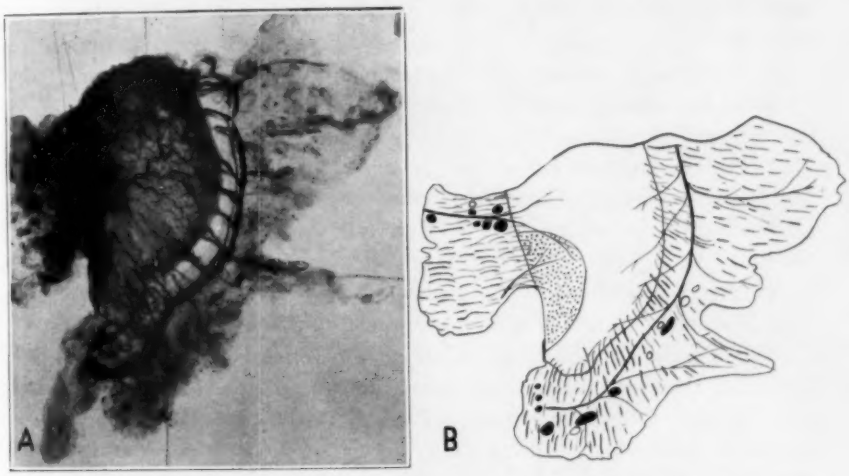

Fig. 1.—*A*, photograph of a cleared specimen. *B*, line drawing of the lymphatic metastases in *A*. Of the 19 lymph nodes isolated, 13 were found to contain microscopic nests of metastatic carcinoma even though not suggestive of metastases grossly.

in the group having no metastases in regional lymph nodes. The largest number of nodes isolated in any one operative specimen was 92, and 14 of these showed evidence of metastatic carcinoma. Of the 13 specimens showing no metastases in lymph nodes, 7 had 13 or less lymph nodes isolated per specimen. Most of the operations in this series were palliative because of extensive local infiltration or poor operative risk (age), and only small segments of the adjacent mesenteries with their included lymph nodes were resected. It is safe to assume that if more of the adjacent supportive tissues had been resected and examined for lymph nodes, involvement of regional lymph nodes

would more closely approximate 88 per cent in this series. Only 6 of the 53 cases (11.2 per cent) were represented by enough lymph nodes to indicate that there were probably no metastases in the regional lymph nodes. Carcinomatous invasion of the submucosal lymph channels of the stomach was present in several of these cases.

For comparison, 55 cases of partial gastric resection for carcinoma, done in 1937 and 1938, were reviewed. The operative specimens had been examined for lymph nodes by gross manual dissection. In 18 of the 55 cases, either lymph nodes were not detected by palpation or, if present, were not thought to be sufficiently suggestive of malignancy to warrant microscopic section, and in only 27 of the 55 cases (49 per cent) was there evidence of metastasis to the regional lymph nodes.

Metastasis to regional lymph nodes is only one factor to be considered in determining the operability and prognosis of carcinoma of the stomach. Inoperability or poor outlook may result from an extensive local infiltration, hematogenic metastases or peritoneal implants. In 15 per cent of the most favorable of the cases in which a partial or subtotal gastric resection was performed, there was microscopic evidence of infiltration into blood vessels, even though gross metastases could not be detected; this was comparable to the 15 per cent microscopic infiltration of blood vessels noted in our study of carcinoma of the rectum. In 47 (88.6 per cent) of the cases the carcinoma had infiltrated completely through the gastric wall and had involved the serosa. This is a constant source of free peritoneal implantation.

The duodenum was involved by the carcinoma in 14 cases (26.4 per cent); in some, by direct extension; in others, through the submucosal and intermuscular lymphatic channels. Careful study of the operative specimens, both the gross specimens and multiple microscopic sections, revealed that in 13 (24.5 per cent) the neoplasm had extended to the upper margin of the resection, usually along the lesser curvature or the posterior wall of the stomach, even though it was impossible to determine this by palpation at the time of operation. It is often difficult to determine by palpation alone the extent of the neoplasm, especially a sessile neoplasm. In this clinic the specimens are now examined grossly as soon as removed, and if any question arises as to the margin of safety, further resection is done.

THE LYMPHATIC DRAINAGE OF THE STOMACH

There are three systems of lymphatics of the stomach: the intramural, the intermediary and the extramural.

Intramural System.—This consists of three networks: the submucosal, the intermuscular and the subserosal. The submucosal lymphatic channels communicate freely with similar channels throughout

the submucosa of the stomach and to a lesser degree with those of the duodenum. They also connect freely with the deeper intermuscular network through radial lymph channels. The intermuscular network is located between the oblique, circular and longitudinal muscle layers. This network communicates with other similar channels as well as draining into the subserosal network found beneath the serosal investment of the stomach.

Intermediary System.—This is made up of numerous small lymph channels between the subserosal network and the extramural collecting systems.

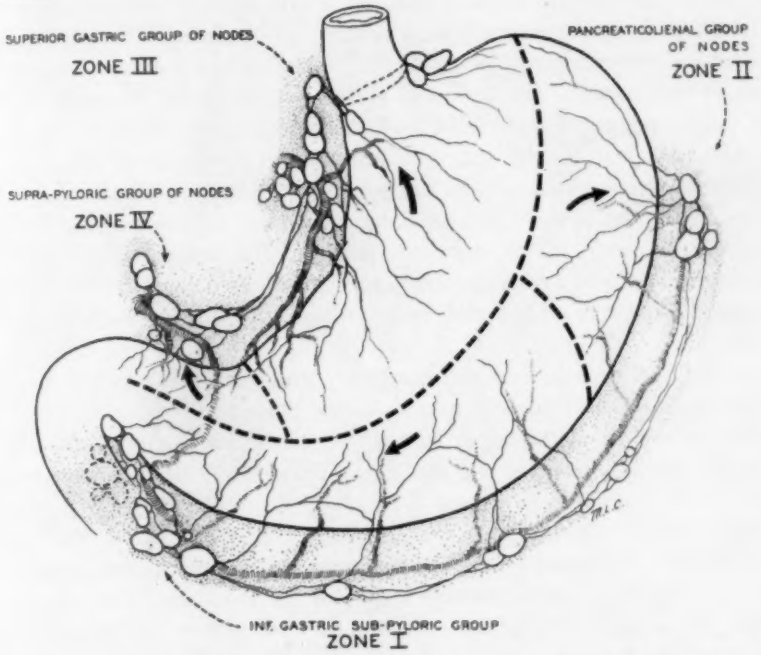

Fig. 2.—Diagrammatic drawing illustrating the zonal lymphatic metastases of carcinoma of the stomach.

Extramural System.—This is comprised of four zones of lymphatic drainage, corresponding largely with the vascular supply of the stomach (fig. 2).

The first zone is the inferior gastric–subpyloric, consisting of a group of nodes and lymphatic channels located in the gastrocolic ligament both above and below the right gastroepiploic vessels. This zone drains the lymph from the pyloric half of the greater curvature of the stomach. The direction of lymph flow is from above downward toward the pylorus and between the head of the pancreas and the second

portion of the duodenum. These lymph channels and nodes accompany the gastroduodenal vessels and eventually drain into the hepatic nodes along the hepatic vessels and into the celiac and aortic nodes. The majority of the nodes in this zone are on the outer aspect of the gastroepiploic vessels, often as much as 3 to 4 cm. from the greater curvature of the stomach. Consequently, any radical removal of these glands must include wide portions of the gastrocolic and duodenocolic ligaments. Residual carcinoma is often left in this zone.

The second zone, or the pancreaticolienal group of glands, is less important, as carcinoma of the stomach in the majority of cases is located in the pyloric antrum and distal one third. However, when it is in the body of the stomach or when the lymph channels of the inferior gastric–subpyloric group are plugged, retrograde metastasis may take place in this zone. This group of nodes and lymphatic channels drains the upper aspect of the cardia and fundus and are found in the gastrocolic and gastrolienal ligaments along the course of the left gastroepiploic vessels. From here their efferent channels drain into the nodes along the splenic vessels lying along the superior aspect of the pancreas. Lymph nodes along the short gastric vessels in the gastropancreatic ligament are occasionally the site of metastases. The efferent channels from the pancreatic nodes drain into the celiac and aortic nodes.

The third zone of lymphatic spread comprises the superior gastric lymph nodes and channels in the lesser omentum following the left gastric artery along the upper two thirds of the lesser curvature. This zone drains the lymph from the lesser curvature half of the stomach except for a small area above the pylorus and the esophageal aspect of the fundus. These nodes are not exactly in the lesser omentum or gastrohepatic ligament but are actually in the ligament containing the left gastric artery which extends from the lesser curvature to the posterior abdominal wall at the celiac axis and above. However, this ligament for the most part is fused with the gastrohepatic ligament, at least at its beginning, and they are usually considered as one. The efferent channels from these nodes for the most part drain to the celiac nodes. The nodes about the cardiac orifice drain somewhat to the esophageal nodes.

The fourth zone includes the suprapyloric nodes, which drain the lymph from the pylorus and the small portion of the lesser curvature of the stomach. The efferent channels of these nodes drain to the hepatic nodes along the hepatic artery and here, in turn, to the celiac and aortic nodes.

Cancer emboli may metastasize in any one or all four zones of lymphatic spread. This fact is beautifully demonstrated by an autopsy specimen in which all the upper abdominal structures about the stomach

were removed, cleared and carefully dissected (fig. 3). The two most important zones of spread appear to be the inferior gastric–subpyloric zone and the superior gastric zone. These are often inadequately excised, because the neoplasm is so extensive that only a palliative procedure is attempted, there are no nodes palpable, or the surgeon is not making a conscientious attempt at complete eradication of the carcinoma. Radical operation for carcinoma of the stomach is different from that for carcinoma in other locations. Many times it is technically impossible to remove much of the adjacent mesentery and ligaments, but extensive

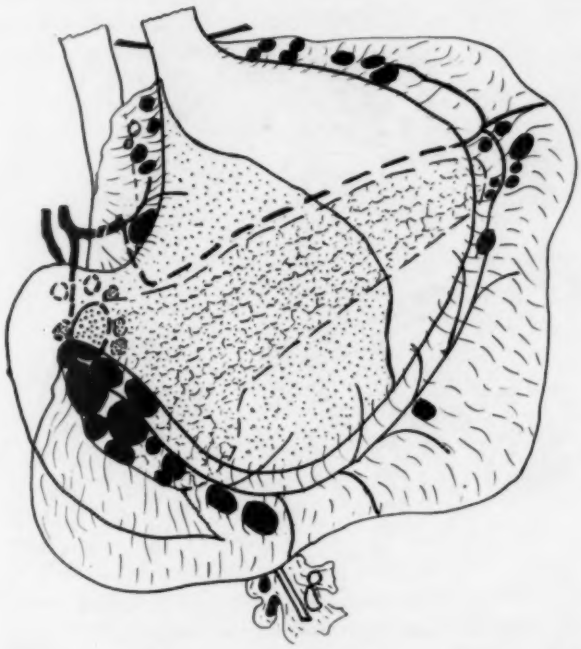

Fig. 3.—Line drawing of an autopsy specimen of carcinoma of the stomach, demonstrating the zonal lymphatic metastases. The extensive nodal metastases to the inferior gastric–subpyloric zone (zone 1) are noted.

removal of as much of the adjacent gland-bearing supportive tissue as possible when the carcinoma is in the early stage and the prognosis favorable is advocated, even though there are no palpable nodes.

Lymphatic vessels differ from blood vessels in that instead of one or two channels draining the same area, the lymph is returned by a number of channels, which tend to form a plexus about the blood vessels. There may also be a number of efferent vessels for any one node; this explains the observation that contiguous lymph nodes may

not be involved. Lymph nodes act as barriers to filter out neoplastic emboli. A neoplastic embolus enters a lymph node by the pericapsular and subcapsular lymph channels. If the metastasis remains viable, it sets up a new neoplastic focus, which tends to block the lymph channel, which then becomes dilated and distended with lymphocytes. The lymph flow becomes static, and other neoplastic foci are often established along the course of the lymph channels. It is therefore quite common to find multiple neoplastic nodules in both the greater and the lesser omentum. The direction of lymph flow determines the direction of lymphatic metastasis. If the lymph channels become plugged with

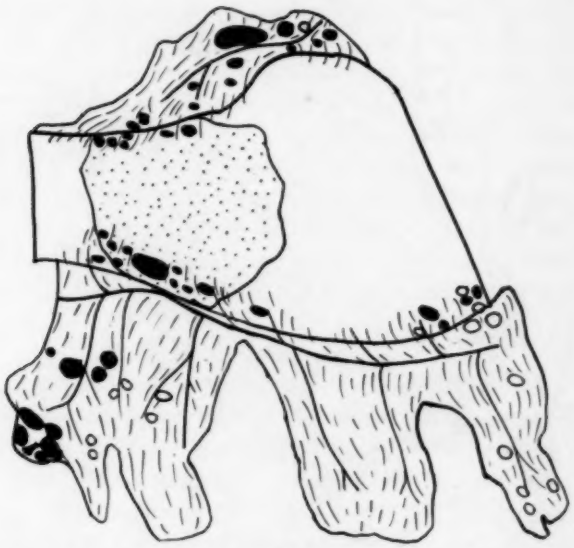

Fig. 4.—Line drawing demonstrating extensive lymphatic metastases of a carcinoma of the stomach after a partial gastric resection.

neoplastic emboli, the lymph will find unobstructed channels, and neoplastic emboli may flow to other zones of the lymphatic spread. In several instances of carcinoma of the pyloric antrum with extensive regional metastasis to the inferior gastric–subpyloric glands, spread to the pancreaticolienal zone took place (fig. 4). The demonstrable zonal distribution in the 40 cases in which there was involvement of regional lymph nodes was as follows: In 34 cases there was lymphatic metastasis to the inferior gastric–subpyloric zone; in 23, to the superior gastric zone; in 12, to the suprapyloric zone; in 7, to the pancreaticolienal zone.

In 5 cases there were four zones of spread; in 4, three zones; in 15, two zones, and in 16, one zone. Of the 34 cases in which there were

metastases to the inferior gastric–subpyloric group, there was involvement of lymph nodes up to the line of resection of the duodenocolic ligament in 21.

In 3 autopsies after partial gastric resection, all the remaining gland-bearing tissues in the four zones of spread were cleared and examined for lymph nodes. In 2 of these, involved nodes were found about the head of the pancreas and the duodenal stump, that is, in zone 1, the inferior gastric–subpyloric zone (figs. 5 and 6).

Fifteen of the 23 cases in which there was metastasis to the regional lymph nodes of the superior gastric zone disclosed involved lymph nodes up to the margin of the excision of the lesser omentum. An insufficient amount of supportive tissue to include any lymph glands was removed

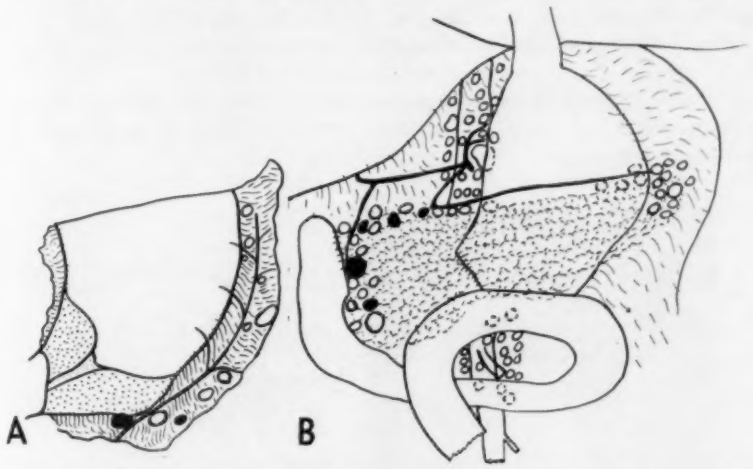

Fig. 5.—*A*, line drawing of the lymphatic metastases of a carcinoma of the stomach, demonstrating the nodal metastases to two lymph nodes in the inferior gastric–subpyloric zone (zone 1) which were close to the line of resection of the gastrocolic ligament. *B*, line drawing of the residual lymphatic metastases in the inferior gastric–subpyloric zone in the autopsy specimen in the same case. Note that there were 5 lymph nodes about the duodenal stump and head of the pancreas (zone 1) that contained residual carcinoma.

along the lesser curvature in 6 cases. Three of these cases were included in the group in which there were no lymph node metastases. Figure 7 illustrates the type of operation that will probably be associated with the largest number of cures and the smallest operative mortality. The entire omentum was removed from this specimen. The duodenocolic ligament was adequately dissected along the duodenum and head of the pancreas, and by this means the one and only involved lymph node was included. The dissection should be carried well posterior on the lesser curvature to include all of the nodes about the left gastric vessels.

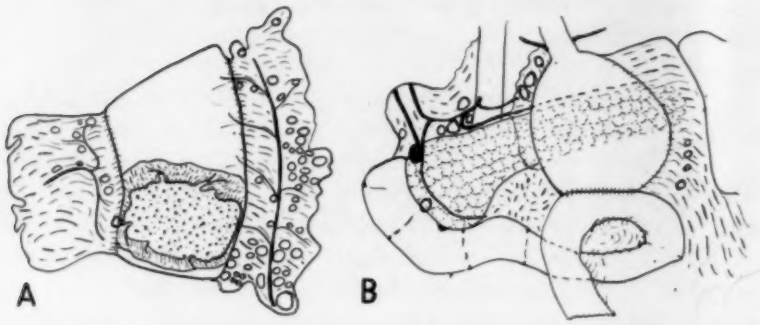

Fig. 6.—*A*, line drawing of the operative specimen in a case of carcinoma of the stomach, demonstrating the absence of nodal metastases even though as many as 60 lymph nodes were isolated. *B*, line drawing of the residual lymphatic metastasis in the inferior gastric–subpyloric zone in the autopsy specimen in the same case. Even though all the susceptible gland-bearing area was thought to have been removed at the time of operation, further examination of the autopsy specimen revealed a single residual metastasis in a lymph node adjacent to the duodenal stump.

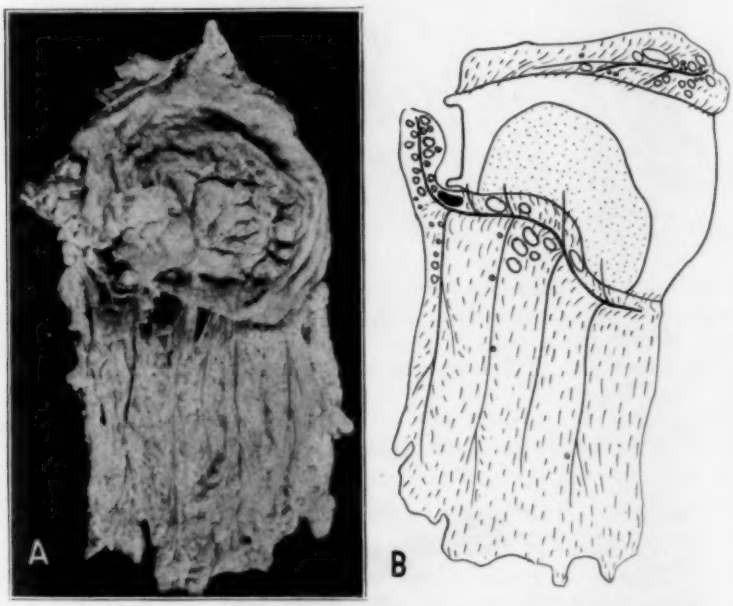

Fig. 7.—*A*, gross operative specimen of a carcinoma of the stomach, illustrating the wide margin of normal gastric wall removed about the lesion and the extensive resection of the adjacent gland-bearing ligaments, mesenteries and omentum. *B*, line drawing of this specimen, demonstrating that as a result of the extensive resection of the inferior gastric–subpyloric zone, the one and only positive lymph node was obtained.

LOCATION OF NEOPLASM WITHIN THE STOMACH IN RELATION TO INCIDENCE AND LOCATION OF METASTASES

In most of the cases in this series the carcinoma was located either in the prepyloric region or in the pyloric antrum. In a number of instances the neoplasm in the pyloric antrum extended into the fundus of the stomach. In 2 cases it extended to the cardia. In 26 cases the carcinoma was completely annular; in 10 it was confined largely to the lesser curvature; in 7, to the anterior wall; in 5, to the greater curvature, and in 5, to the posterior wall. The incidence of metastases from carcinoma in these various locations, as well as the incidence of metastases in the various zones of lymphatic spread, is shown in table 1.

The conclusions to be drawn from table 1 are: (1) annular carcinoma is likely to spread to all zones; (2) a small neoplasm on the lesser curvature may metastasize to the nodes along the greater curvature;

TABLE 1.—*Local and Zonal Incidence of Metastasis*

Location	Cases	Cases in Which Metastases Occurred	Zone of Metastasis			
			Inferior Gastric-subpyloric	Pancreatico-lienal	Superior Gastric	Supra-pyloric
Annular	26	22	22	5	14	9
Lesser curvature	10	5	5	0	5	1
Anterior wall	7	6	6	0	3	0
Greater curvature	5	3	3	1	0	1
Posterior wall	5	4	4	1	1	1

(3) a small neoplasm on the greater curvature may metastasize to the nodes along the lesser curvature; (4) a neoplasm located on either the anterior or the posterior wall may metastasize to the nodes along either curvature. Consequently, wide margins of the gland-bearing supportive tissues should be excised along both curvatures of the stomach, regardless of the location of the neoplasm.

SEX AND AGE IN RELATION TO LYMPHATIC METASTASIS

Metastasis to regional lymph nodes occurred in 35 of the men (77.7 per cent) and in 5 of the 8 women (62.5 per cent).

The average age of all the patients was 57.7 years. The average age of those with metastases was 57.2 years, in comparison with 59.7 years for those without. The 2 youngest patients were 40 and the oldest was 81 years of age. There were 13 below 50 years of age, 77 per cent of whom had metastases. There were 40 above 50 years, of whom 75 per cent had metastases. Age is not a factor in determining the incidence of metastases.

DURATION OF SYMPTOMS AND LYMPHATIC METASTASIS

The average duration of symptoms was thirteen and one one-hundredth months. For the group without metastases there was an average duration of thirteen and forty-five hundredths months; for the group with metastases it was twelve and eighty-seven hundredths. This difference is not striking, but it again emphasizes the fact that long duration of symptoms does not necessarily make the carcinoma inoperable or the prognosis less favorable. There were 5 patients with symptoms for over one year who were found to be free from regional lymphatic metastases. Several of these had been ill for two and three years. On the other hand, there were 6 patients whose symptoms had ranged from one to three months and who subsequently were found to have lymphatic metastases. Duration of symptoms alone should not influence the treatment advised.

SIZE OF NEOPLASMS AND LYMPHATIC METASTASIS

There was no relation between the size of the neoplasm and the presence of metastases. The largest neoplasm was 14 cm. in length and had not metastasized. The smallest neoplasm was 2 cm. in length and had metastasized. The average size was 7.37 cm. in length. Of the 26 neoplasms larger than average, 22 (84.7 per cent) had metastasized, compared to 18 (66.6 per cent) of the 27 lesions smaller than average. Five of the 6 largest neoplasms and 4 of the 6 smallest neoplasms were found to have metastasized. This emphasized the fact that radical operative resection should be done in patients having small tumors. Figure 8 illustrates a small carcinoma which at the time of operation was thought to be a large callus ulcer that had extensive metastases in the regional lymph nodes even though no palpable lymph nodes existed.

GROSS TYPE AND LYMPHATIC METASTASIS

The gastric carcinomas in our series were classified by their gross characteristics into three groups. The first group included 6 neoplasms which on gross examination were thought to be ulcers. Two of these were subsequently found to have resulted from carcinomatous proliferation at the edges of peptic ulcers, whereas a third accompanied two nearby peptic ulcers; the remainder were small ulcerating carcinomas. The second group included the sessile or plaquelike neoplasms which tended to infiltrate the wall of the stomach. The third group consisted of the large polypoid fungating neoplasms, many of which had ulcerating centers. A correlation of the gross types with lymphogenous metastases (table 2) shows (except for the ulcerating type) that the polypoid fungating neoplasms are less malignant than the sessile neoplasms. Five

of the 6 carcinomas infiltrating into muscle only were polypoid in character, and 2 had arisen on ulcers.

There were metastases in 4 (66.6 per cent) of the 6 cases of the ulcer type, too small a number from which to draw conclusions. However, 21 (95.4 per cent) of the 22 sessile carcinomas had metastasized, compared with 15 (60 per cent) of the 25 polypoid neoplasms. This emphasizes the highly malignant character of the sessile carcinomas.

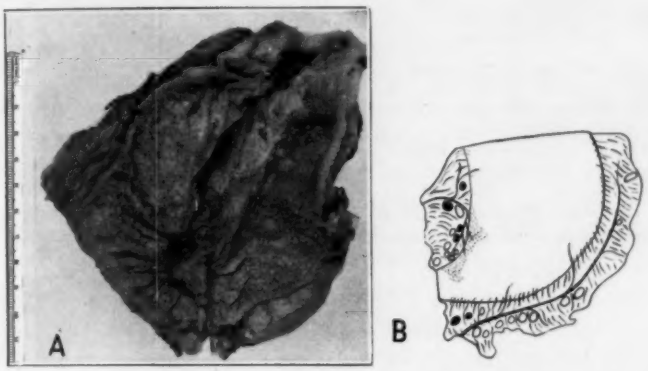

Fig. 8.—*A*, gross specimen of a carcinoma of the stomach following partial gastric resection, demonstrating a small ulcerated neoplasm of the lesser curvature near the pylorus. *B*, line drawing of the lymphatic metastases from the carcinoma in this specimen, demonstrating the large number of involved lymph nodes, even though this was not clinically suggested.

TABLE 2.—*Gross Types of Carcinoma Correlated with Lymphatic Metastasis*

Gross Type	Cases	Cases in Which Metastases Occurred	Per Cent
Ulcerous	6	4	66.6
Sessile	22	21	95.4
Polypoid	25	15	60.0

DEPTH OF INFILTRATION AND LYMPHATIC METASTASIS

Forty-seven of the 53 neoplasms had extensively infiltrated through the entire stomach wall and involved the serosa. Thirty-eight of these (80.8 per cent) had given rise to demonstrable metastases in regional lymph nodes. In 2 of the 5 specimens (40 per cent) in which the carcinomatous infiltration was confined to the muscular layer metastases were also found. The single carcinoma in which infiltration had extended into the submucosa only had not metastasized. Thus, the more extensive the depth of infiltration, the greater the possibility of metastasis to the regional lymph nodes.

DEGREE OF CELLULAR DIFFERENTIATION (GRADING) AND LYMPHATIC METASTASIS

The majority (31) of the carcinomas of the stomach were graded 3 as to cellular differentiation. There were 11 carcinomas graded 2 and 10 that were graded 4. Only 1 carcinoma was graded 1, and it showed shallow infiltration at the base of a gastric polyp. Table 4 substantiates the dictum that the more anaplastic the neoplasm, the more likely the presence of lymphatic metastases.

TABLE 3.—*Depth of Infiltration and Lymphatic Metastasis*

Depth of Infiltration	Cases	Cases in Which Metastases Occurred	Per Cent
Entirely through wall, with involvement of serosa	47	38	80.8
Infiltration into muscle layers	5	2	40.0
Infiltration into submucosa	1	0	0

TABLE 4.—*Cellular Differentiation and Lymphatic Metastasis*

Grade	Cases	Cases in Which Metastases Occurred	Per Cent
1	1	0	0
2	11	7	63.33
3	31	24	77.41
4	10	9	90.00

TABLE 5.—*Microscopic Type and Metastasis*

Type	Cases	Cases in Which Metastases Occurred	Per Cent
Medullary adenocarcinoma	6	6	100
Scirrhous adenocarcinoma	4	4	100
(a) Partly papilliferous	1	1	100
(b) Partly adenocarcinoma mucosum	5	5	100
(c) Partly adenocarcinoma	4	4	100
Adenocarcinoma mucosum	7	6	85.71
(a) Partly papilliferous adenocarcinoma	1	1	100
Adenocarcinoma (simplex)	16	9	56.25
(a) Partly adenocarcinoma mucosum	2	1	50
Papilliferous adenocarcinoma	7	3	42.85
Total	53	40	75.5

MICROSCOPIC TYPE AND LYMPHATIC METASTASIS

In table 5 it will be noted that the neoplasms were distributed evenly among the various types except for adenocarcinoma (simplex). Medullary adenocarcinoma and scirrhous adenocarcinoma had the highest

incidence of metastases (100 per cent), and the tumors belonging to these types were all graded either 3 or 4, again showing that they tended to be more malignant. The type having the next highest incidence (85.7 per cent) of metastases was adenocarcinoma mucosum. The two types showing the least incidence of metastases were adenocarcinoma (simplex) (56.25 per cent) and papilliferous adenocarcinoma (42.85 per cent).

SUMMARY

An analysis of the incidence of metastases in regional lymph nodes in 53 cases of carcinoma of the stomach is presented.

As a result of the special method used in the investigation, evidence of metastases was found in 75.5 per cent of the cases in this study. This figure would more closely approximate 88 per cent if more nodes could have been obtained in cases in which operation was done for palliation alone.

Gastric carcinoma had involved the duodenum in 26.4 per cent of the cases.

The upper margin of the neoplasm in 24.5 per cent could not be determined by palpation alone at the time of operation.

The most important zones of lymphatic metastases are the inferior gastric–subpyloric and the superior gastric. Frequently, carcinomatous nodes are left in these zones even though all gross evidence of malignancy is removed.

There was no relation between duration of symptoms and lymphatic metastases.

There was no relation between the size of the neoplasm and the presence of lymphatic metastases. Small neoplasms were often associated with extensive nodal metastases.

Of the sessile neoplasms, 95.4 per cent had metastasized, in comparison with 60 per cent of the polypoid neoplasms.

The more anaplastic the carcinoma cells were, the higher the incidence of metastases was.

Medullary adenocarcinoma, scirrhous adenocarcinoma and adenocarcinoma mucosum were associated with the highest incidence of metastases. Adenocarcinoma (simplex) and papilliferous adenocarcinoma were associated with the lowest incidence of metastases.

In the majority of cases of carcinoma of the stomach in which the regional nodes were not palpable or, if palpable, were not thought to be suggestive of malignancy, the carcinoma was subsequently shown to have metastasized.

Whether palpable lymph nodes are present or not, the four zones of lymphatic metastases should be included within the resection to increase the likelihood of cure.

ACUTE CHOLECYSTITIS

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AND
ARTHUR W. ALLEN, M.D.
BOSTON

During the ten year period following Jan. 1, 1930 there were 2,273 patients operated on for nonmalignant extrahepatic disease of the biliary tract in the Massachusetts General Hospital, exclusive of the Phillips House private ward. Of this number, 415 patients, or 18.25 per cent of the whole, had acute cholecystitis. We selected the cases of these patients for study after a careful review of all the records. In every case the diagnosis was supported not only by the operator's opinion but by the pathologic report. All patients had symptoms of acute disease. In 85 per cent pain, tenderness, spasm, palpable mass, a temperature above 101 F. and a leukocyte count above 12,000 were present; with respect to the other 15 per cent, one or another of these findings was not recorded. The most common omission was the presence of a mass in the upper right quadrant of the abdomen. In every instance we were satisfied that the diagnosis was substantiated; if there was doubt, the case was excluded. Thus in 97 additional cases the disease was reported as acute, but the other requisites for the diagnosis were lacking. Many other cases in which the disease was considered acute by the operator were also excluded for the same reasons. We therefore believe that this report accurately represents our experience with acute inflammation of the gallbladder during the period under consideration.

In previous reports [1] we have shown that the mortality rate of simple cholecystectomy in this whole group of patients with chronic subacute and acute disease of the gallbladder was 2.45 per cent. If those whose disease was acute are eliminated, the mortality rate was 1.74 per cent. In those patients who underwent exploration of the common duct and who were found to have stones in the duct the mortality rate was 7.16 per cent; while in those who had exploration of the common duct with a negative result in addition to cholecystectomy the mortality was 2.04 per cent. In these 415 patients with acute cholecystitis the operative

From the Surgical Service of the Massachusetts General Hospital.

1. Allen, A. W., and Wallace, R. H.: Technic of Operation on the Common Bile Duct, Am. J. Surg. **28**:533-561 (June) 1935; The Surgical Management of Stone in the Common Bile Duct, Ann. Surg. **111**:838-847 (May) 1940.

mortality rate was 6.06 per cent. We are interested in determining if possible the factors influencing the morbidity and the mortality in these cases of acute cholecystitis. Much has been written concerning the matter but one feels that in many instances the classification of the disease process was not clear. This makes for confusion and has caused strong advocation of immediate or early operation, on one hand, and delayed operation, on the other. Consideration of the time element has usually been restricted to the time after entry into the hospital with no attention given to the duration of the disease. Attempts have been made to emphasize the danger of gangrene and perforation. Some have stressed the desirability of cholecystectomy rather than cholecystostomy. It is our hope that the analysis of our cases will help to clarify some of these disputed points.

THE AGE FACTOR

Sanders [2] and others have called attention to the fact that the operative mortality rate of disease of the gallbladder is higher in older

TABLE 1.—*Age Incidence and Mortality in 415 Cases of Acute Cholecystitis*

Age Group	Cases	Deaths	
		Number	Per Cent
Under 40	80	1	1.2
40 to 49	115	5	4.3
50 to 59	123	11	8.9
60 to 69	69	7	10.1
Over 70	28	1	3.5

patients. This we believe has a dual meaning. The younger patient has fewer complicating disorders, but the older patient, on the other hand, has usually had infection of the biliary tract for a longer period of years and thus has more damage of the liver. This is an excellent argument against palliative management of disease of the gallbladder, especially when there are stones in the common duct. The risk of cholecystectomy in the early stages of the disease is far less than the risk of future trouble necessitating surgical intervention at a time when the hazard of operation is greatly increased. In 25 per cent of our patients, however, the first attack of acute pain was associated with acute cholecystitis. This we believe is an argument against delaying operation on the basis of a first attack.

Table 1 gives the age distribution in our cases together with the mortality rates. Table 2 gives the mortality statistics for those cases in which the patients were under and those in which the patients were

2. Sanders, R. L., in discussion on papers of Heyd, Parsons and Allen and Wallace, Tr. South. S. A. **52**:182, 1939.

over 45 years of age. The 2 deaths in the younger group were due to massive pulmonary emboli; this was confirmed at autopsy in both instances.

GANGRENE AND PERFORATION

Since it has long been known that gangrene of the gallbladder often follows acute cholecystitis and that rupture of the gallbladder frequently takes place under these circumstances, we have analyzed our cases in

TABLE 2.—*Mortality Statistics in Cases in Which the Patients Were Under and in Cases in which the Patients Were Over 45*

	Under 45	Over 45
Cases	139	276
Deaths		
Number	2	23
Per cent	1.44	8.33

TABLE 3.—*Operative Mortality in Relation to Presence or Absence of Gangrene*

	Cases	Deaths	
		Number	Per Cent
Gangrene absent	292	11	3.75
Gangrene present	123	14	11.50
Total	415	25	6.06

TABLE 4.—*Operative Mortality in Relation to Presence or Absence of Perforation*

	Cases	Deaths	
		Number	Per Cent
Perforation absent	59	3	5.3
Perforation present	64	11	17.2
Total	123	14	11.5

regard to these factors. That the operative mortality is higher in the presence of gangrene with perforation is established, notwithstanding the infrequency of generalized peritonitis accompanying this complication. At the time of operation gangrene of the gallbladder was present in 29.4 per cent of all cases of acute cholecystitis, and in over half of these it had perforated the gallbladder. In 3 of these the process had perforated into the free peritoneal cavity, and there was general peritonitis at the time of operation.

The data shown in tables 3 and 4 indicate that operation for acute cholecystitis with or without gangrene is accompanied by a reasonably satisfactory mortality rate, unless perforation has taken place.

Inasmuch as gangrene with perforation occurs so frequently and is associated with such a high mortality rate, we attempted to find some indications by which these complications could be predicted. The age distribution of these cases as compared with the entire group is shown in chart 1 and eliminates the possibility of any help from this source.

The maximum temperature and the maximum leukocyte count, shown in tables 6 and 7, are likewise unreliable guides to the state of the disease process.

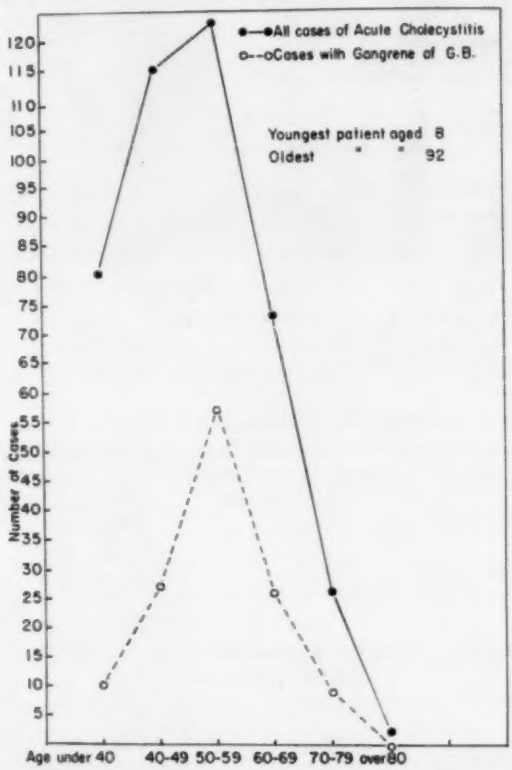

Chart 1.—Similarity of age distribution of acute cholecystitis to that of gangrene of the gallbladder. The peak appears in the fifth decade.

THE FACTOR OF DURATION OF SYMPTOMS

This factor was analyzed in relation to the mortality rate in all cases. Those in which there was gangrene and those in which there was gangrene with perforation were reviewed separately in this respect (chart 2).

Gangrene occurred prior to the fourth day of the disease in only 10 instances. There was no case in which perforation occurred prior to

this time, and there were only 3 instances in which it occurred between the fourth and the sixth day after onset; all 3 of the patients recovered.

The average duration of symptoms before operation for all 415 cases of acute cholecystitis was eight and nine-hundredths days (chart 3). In

TABLE 5.—*Operative Mortality in Relation to Abscess, Local Peritonitis and General Peritonitis Following Perforation*

	Cases	Deaths	
		Number	Per Cent
Perforation with abscess	52	8	15
Perforation with local peritonitis	9	0	0
Perforation with general peritonitis	3	3	100
Total	64	71	17.2

TABLE 6.—*Maximum Preoperative Temperature*

	Temperature Over 102 F.		Temperature Over 103 F.	
	Number	Per Cent	Number	Per Cent
All cases (415)	202	48.6	88	21.2
Cases with gangrene (123)	58	47.1	24	19.5

TABLE 7.—*Maximum Preoperative Leukocyte Count*

	Leukocyte Count Over 20,000	
	Number	Per Cent
All cases (415)	106	25.5
Cases with gangrene (123)	41	33.3

TABLE 8.—*Operative Mortality in Relation to the Duration of Symptoms Before Operation*

	Cases	Deaths	
		Number	Per Cent
4 days or less	108	3	2.77
5 to 8 days	133	9	6.78
9 days or more	174	13	7.47

26 per cent of the cases operation had been performed by the fourth day of the disease; in 42 per cent there was a delay of nine days or more after symptoms appeared before operation was undertaken.

Among the 108 cases in which operation was performed by the fourth day after the onset of the disease there were 3 deaths, 2 from post-operative pneumonia and 1 from pulmonary embolism. The mortality rate increased materially after this time. During the period covered by

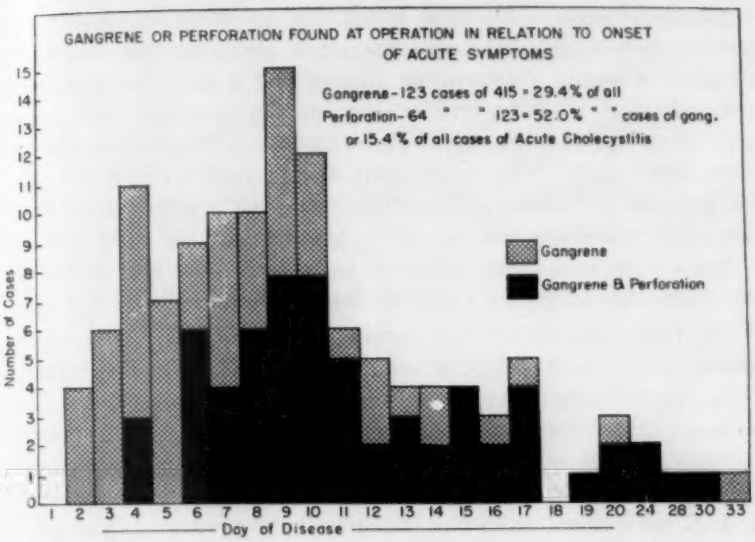
GANGRENE OR PERFORATION FOUND AT OPERATION IN RELATION TO ONSET OF ACUTE SYMPTOMS
Gangrene-123 cases of 415 = 29.4% of all
Perforation-64 " " 123 = 52.0% " " cases of gang.
or 15.4 % of all cases of Acute Cholecystitis
Gangrene
Gangrene & Perforation
Number of Cases
Day of Disease

Chart 2.—Duration of disease at operation when gangrene or gangrene together with perforation was found. In the cases of perforation before the sixth day after the onset of symptoms the perforations were all early, and all 3 patients recovered.

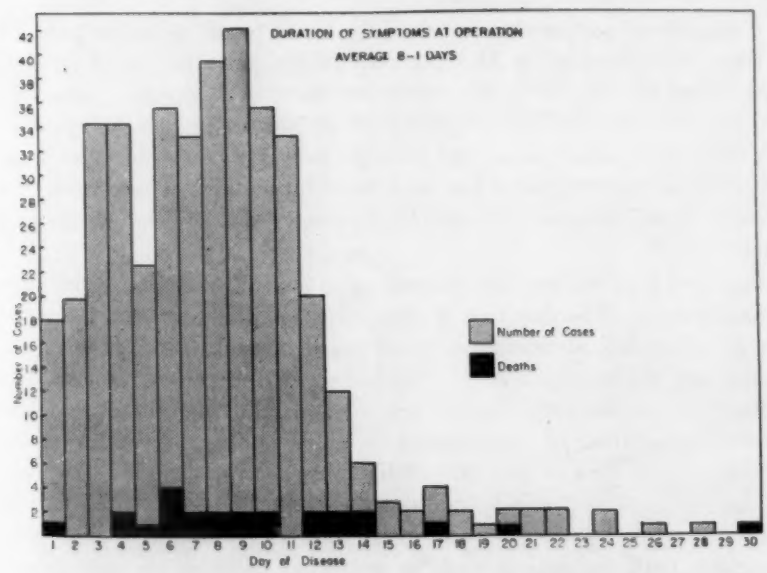

Chart 3.—Duration of disease at operation and deaths in all cases of acute cholecystitis. The 3 deaths of patients operated on within four days after onset of symptoms were not directly related to the primary disease.

this study the majority of the hospital staff favored delayed operation in acute cholecystitis. We must admit that we were strong advocates of careful observation of the patients and of operating only when there was failure of steady improvement, hoping that a subacute phase might be reached, which we felt offered a safer time for operation. We thought that by so doing we could avoid cholecystostomy and remove the gallbladder more often. Also we believed that perforation, if it did occur, would produce a localized process that would not greatly interfere with an adequate procedure and recovery. Miller [3] felt that early operation was desirable in such cases, although he had not been able at the time of his publication to gather sufficient data to support his view strongly.

Forty-four patients in this group were subjected to emergency operation within four hours of admission to the hospital. Seventeen of these were operated on after a mistaken diagnosis, 11 for acute appendicitis and 6 for perforated peptic ulcer. There were 4 deaths in this group, 2 from general peritonitis present at the time of operation and 2 from pulmonary complications after lengthy surgical procedures. Thus it is not evident from our statistics that emergency operation for acute cholecystitis is particularly hazardous, since 2 of the patients would certainly not have benefited by delay. It is evident to us all, however, that delay is indicated until chemical balance and hydration have been cared for. Since an adequate team is important, this operation is a poor one for the middle of the night.

Certainly we cannot place much of the blame for delay on our patients, or their physicians, since 71.3 per cent of the patients sought relief in the hospital by the fourth day after the onset of symptoms (chart 4). The average duration of symptoms on admission for all 415 patients was three and a half days; the average period of hospital delay from admission to operation was four and three-fifths days. There were only 3 deaths in the series which could be considered due to delay on the part of the patient.

Our policy of waiting has allowed us to study the results of this type of management. The duration of symptoms on admission and the duration of symptoms at operation of all cases of perforation of the gallbladder are shown in chart 5. Thirty-four of the patients entered the hospital before the fifth day of symptoms, and 30 of these doubtless suffered perforation of the gallbladder while under observation in the hospital. Since we can find no reliable criteria to indicate the presence of gangrene and perforation, we must change our policy from one of watchful waiting to one of operating as soon as the optimum conditions as regards both the patient and the operating facilities are established.

3. Miller, R. H.: Acute Cholecystitis, Ann. Surg. **92**:644-648 (Oct.) 1930.

CHOLECYSTECTOMY AND CHOLECYSTOSTOMY

We realize that there are many factors not taken account of in a study of records and that the evidence pointing to cholecystectomy as

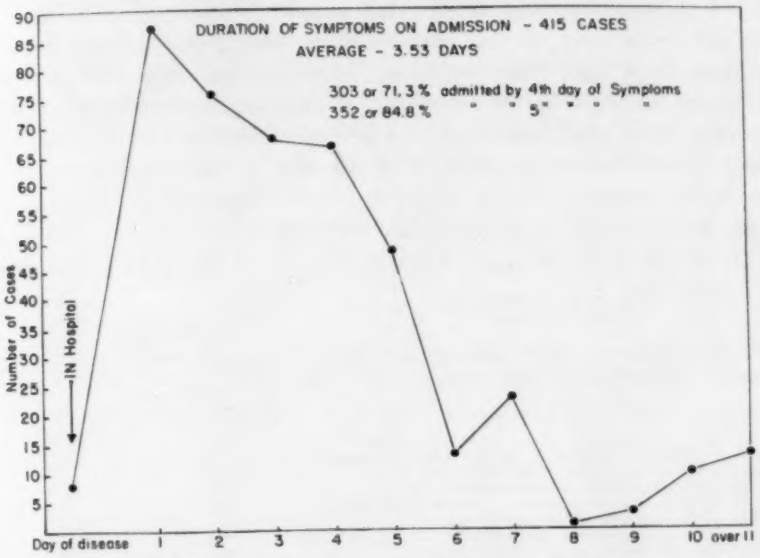
DURATION OF SYMPTOMS ON ADMISSION - 415 CASES
AVERAGE - 3.53 DAYS
303 or 71.3% admitted by 4th day of Symptoms
352 or 84.8% " " 5" " " "
Number of Cases
IN Hospital
Day of disease
1 2 3 4 5 6 7 8 9 10 over 11

Chart 4.—Duration of symptoms on admission. Most patients sought early relief at the hospital.

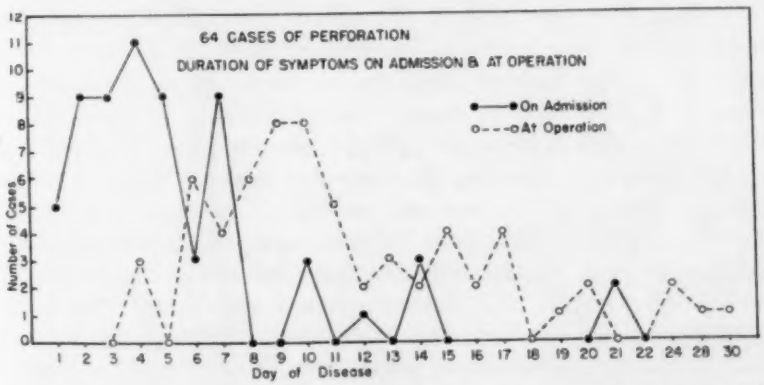
64 CASES OF PERFORATION
DURATION OF SYMPTOMS ON ADMISSION & AT OPERATION
On Admission
At Operation
Number of Cases
Day of Disease
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 24 28 30

Chart 5.—Duration of symptoms on admission and at operation of all patients with perforated gallbladders. The majority were admitted early and were operated on late. Forty-three patients were admitted by the fifth day after the onset of symptoms.

a safer procedure than cholecystostomy is probably subject to much criticism.

Subsequent cholecystectomy was performed on 27 of 127 patients who survived cholecystostomy; there were 3 deaths, a mortality rate of 11.1 per cent for secondary cholecystectomy. In addition, 12 patients had typical biliary colic, and 6 had persistent sinus and refused operation. It is probable that others had secondary operations elsewhere. Only 28.3 per cent of the patients were discharged as well before seventeen days after cholecystostomy, in comparison with 59.3 per cent discharged as well before seventeen days after cholecystectomy. Of survivors after cholecystectomy, 14 per cent remained in the hospital longer than twenty days, while 39.3 per cent of survivors after cholecystostomy remained in the hospital longer than twenty days. It is reasonable that the removal of an infected or gangrenous structure greatly enhances the recovery of the host. Table 9 shows various figures for comparison.

TABLE 9.—*Comparative Data on Cholecystectomy and Cholecystostomy*

	Cholecystectomy	Cholecystostomy
Average age of patients	50.1	55.2
Average duration of symptoms before admission (days)	3.5	3.5
Average delay of operation after admission (days)	4.8	4.1
Patients with preoperative temperature of 103 F.	43	45
Patients with preoperative leukocyte count over 20,000	55	51
Patients with gangrene of the gallbladder	68	55
Patients with gangrene with perforation of the gallbladder	24	40
Average stay of survivors in hospital (days)	18.0	26.1
Mortality rate (per cent)	3.3	11.1
Total number of cases	272	143

As more than one third of all patients were subjected to cholecystostomy, we were interested in whether or not they were chiefly those who delayed hospital admission or were old or debilitated or extremely ill. The records showed that 58 per cent of them entered the hospital within three days after the onset of symptoms and 73.4 per cent within four days after the onset of symptoms. This is a greater percentage of early admissions than was found for those patients who had cholecystectomy. Only 50 of 143 patients who had cholecystostomy were over 60 years of age, and fewer patients with preoperative temperatures over 103 F. and leukocyte counts over 20,000 had cholecystostomy than cholecystectomy. Undoubtedly cholecystostomy was a life-saving measure in numerous cases, but there is no evidence that the majority of the patients were poorer risks than those who had their gallbladders removed. There was a preoperative hospital delay of three days or longer for 53 per cent of patients who had cholecystostomy, and we believe that many of this group could have safely had their gallbladders removed if they had been operated on at an earlier stage of the disease, when the state of inflammation offers much less technical difficulty.

We believe that drainage of the gallbladder with the area under local anesthesia is indicated for the feeble or gravely ill patient and that operation early in the disease will make this an infrequent procedure.

There was no record of stone in the gallbladder in 5.3 per cent of all cases, but no definite mention of absence or failure to find stones was made in many of these cases.

Diabetes requiring insulin was found in 6 per cent of all cases, and the mortality rate in this group was 8 per cent.

Jaundice was present at operation in 45 patients; 16 of these had one or more stones removed from the common duct. Jaundice cleared

TABLE 10.—*Chief Cause of Death*

Cause	Cases	Cause	Cases
Peritonitis	10	Cerebral hemorrhage	1
Pneumonia	7	Hepatic infarct	1
Pulmonary embolus	4		
Cardiac failure	2	Total	25

TABLE 11.—*Complications Necessitating Hospitalization for More than Twenty Days*

Complication	Cases
Wound infection	43
Prolonged fever without explanation	11
Thrombophlebitis	11
Wound dehiscence	4
Pneumonia	2
Prolonged drainage of bile	5
Cardiac lesions	3
Subdiaphragmatic abscess	2
Residual abdominal abscess	1
Miscellaneous	5
No explanation (mostly private cases)	15
Total	102

spontaneously in 29 patients without removal of a stone from the common duct. In 6 of these, no abnormalities were found on exploration of the common duct. Exploration of the common duct was performed on 28 patients who had cholecystectomy; there were 2 deaths, a mortality rate of 7.1 per cent. Exclusive of cases in which operation was performed on the common duct there were 244 in which cholecystectomy was done; there were 7 deaths, a mortality rate of 2.9 per cent.

The average postoperative hospital period for survivors was nineteen days. Of all patients, 46.5 per cent were discharged as well before seventeen days, and 22.5 per cent of the survivors remained in the hospital longer than twenty days.

The chief causes of death are shown in table 10; peritonitis was the most common cause.

Complications of survivors which necessitated hospitalization for more than twenty days are shown in table 11.

SUMMARY AND CONCLUSIONS

Gangrene and perforation are the factors which most strikingly increase the operative mortality in acute as compared with nonacute cholecystitis.

With conservative treatment, even under careful observation in the hospital, gangrene with perforation cannot be anticipated and frequently progresses to a dangerous stage.

Gangrene with perforation is unusual before the sixth day after the onset of symptoms.

Operation within four days of the onset of symptoms is relatively safe if there has been proper preoperative preparation.

Cholecystectomy is the procedure of choice.

Early intervention would practically eliminate the hazard of gangrene with perforation in the patients coming to the hospital.

ALIMENTARY AZOTEMIA AND THE BLEEDING PEPTIC ULCER SYNDROME

C. FRANK CHUNN, M.D.

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AND

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DETROIT

Since 1933, when Sanguinetti [1] first called attention to increased amounts of urea nitrogen in the blood of patients with bleeding peptic ulcer, this observation has been confirmed by many writers. These include Sanguinetti himself [2] (1933), Christiansen [3] (1935, 1936, 1937), Ingegno [4] (1935), Meyler [5] (1935, 1936), Sučić [6] (1935), Alsted [7] (1936), Borst [8] (1936, 1938), Clausen [9] (1936) and Polack [10] (1936).

From the Department of Surgery, Henry Ford Hospital.

Read before the Section on Pathology and Physiology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 6, 1941.

1. Sanguinetti, L. V.: Curvas azohemicas en las hemorragias retenidas del tubo digestivo, Arch. argent. de enferm. d. ap. digest. y de la nutrición **9**:68-75 (Oct.-Nov.) 1933; cited by Schiff and others.[35]

2. Sanguinetti, L. V.: Azoemias en el curso de las hemorragias retenidas a nivel del tubo digestivo (estudio clínico y experimental), Arch. argent. de enferm. d. ap. digest. y de la nutrición **9**:264-287 (Feb.-March) 1934.

3. Christiansen, T.: (*a*) Uraemia as Cause of Death in Massive Haemorrhage from Peptic Ulcer, Acta med. Scandinav. **85**:333-345, 1935; (*b*) Hyperazotaemia in Intraintestinal Haemorrhage, ibid., 1936, supp. 78, pp. 894-899; (*c*) Biochemical Changes in the Organism Produced by Massive Intra-Intestinal Hemorrhage, Rev. Gastroenterol. **4**:166-180 (Sept.) 1937.

4. Ingegno, A. P.: The Elevated Blood Urea of Acute Gastro-Intestinal Hemorrhage and Its Significance, Am. J. M. Sc. **190**:770-774 (Dec.) 1935.

5. Meyler, L.: (*a*) Post-Haemorrhagic Uraemia, Acta med. Scandinav. **87**: 313-325, 1935; (*b*) Uraemia Due to Dehydration, ibid. **90**:475-488, 1936.

6. Sučić, D.: Akute Azotämie bei grossen gastrointestinalen Blutungen, Klin. Wchnschr. **14**:1316-1318 (Sept. 14) 1935.

7. Alsted, G.: (*a*) Studies on Azotaemia After Haematemesis and Melaena, Acta med. Scandinav., 1936, supp. 78, pp. 900-907; (*b*) Further Studies on Azotemia Following Hemorrhage in the Digestive Tract, Am. J. M. Sc. **192**: 199-208 (Aug.) 1936.

8. Borst, J. G. G.: (*a*) Ueber Erhöhung des Kochsalz- und Harnstoffgehaltes und Erniedrigung des Albumingehaltes des Blutes bei Patienten mit starken Magenblutungen, Ztschr. f. klin. Med. **130**:75-96, 1936; (*b*) The Cause

(Footnotes continued on next page)

There have been at least sixteen other reports during the past five years; these will be quoted later. Although this syndrome has apparently been recognized over a period of only eight years, it is of considerable importance. The time has come to take stock and to appraise the significance, cause and mechanism of this syndrome.

SIGNIFICANCE OF AZOTEMIA

In some early studies the opinion was expressed that renal or hepatic damage was the cause of the elevation in urea nitrogen content of the blood accompanying bleeding peptic ulcer. If renal or hepatic damage is the cause, operation is contraindicated. If, on the other hand, azotemia is due to the presence of blood in the intestinal tract, its continuance indicates persistent bleeding and in a doubtful case perhaps argues for surgical intervention. The whole question of operative treatment of bleeding peptic ulcer is so debatable at present that any added information that offers aid in making this difficult decision is of value.

Prognostic Value.—Independent of its importance as a therapeutic guide, azotemia seems to be of definite prognostic import in cases in which operation has not been performed. Witts [11] (1937) and Ingegno [4] (1935) both expressed their belief that the presence of azotemia is of prognostic significance. Ingegno stated: "Persistent elevation may point to persistent hemorrhage." Christiansen [3e] (1937) also stated his opinion that azotemia is of prognostic value; he said: "A slight or transitory rise in the blood urea concentration is suggestive of a good prognosis, whereas high blood urea values—eventually increasing progressively—are to be looked upon as a poor prognostic sign." Yuile and Hawkins [12] (1941) did not credit azotemia with much value in prognosis.

Schiff and Stevens [13] (1939), on the other hand, stated that "its value in prognosis should, in turn, make it an aid to therapeutic manage-

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of Hyperchloremia and Hyperazotemia in Patients with Recurrent Massive Hemorrhage from Peptic Ulcer, Acta med. Scandinav. **97**:68-88, 1938.

9. Clausen, J.: Hyperazotemia in Cases of Acute Ventricle Hemorrhage, Acta med. Scandinav., 1936, supp. 78, pp. 908-914.

10. Polack, E.: Azotemia After Hematemesis, Acta med. Scandinav., 1936, supp. 78, pp. 914-915.

11. Witts, L. J.: Haematemesis and Melaena, Brit. M. J. **1**:847-852 (April 24) 1937.

12. Yuile, C. L., and Hawkins, W. B.: Azotemia Due to Ingestion of Blood Proteins: Blood Urea Increase Related to Ingestion of Whole Blood, Red Cells, Plasma and Other Proteins, Am. J. M. Sc. **201**:162-167 (Feb.) 1941.

13. Schiff, L., and Stevens, R. J.: Elevation of Urea Nitrogen Content of the Blood Following Hematemesis or Melena, Arch. Int. Med. **64**:1239-1251 (Dec.) 1939.

ment" and that "the urea nitrogen content of the blood should be repeatedly estimated in all cases of hematemesis or melena because of its prognostic significance."

Schiff [14] (1940) especially emphasized the prognostic significance of an increase of the urea nitrogen content of the blood after hematemesis and melena. In a series of 135 cases, the urea nitrogen was found to exceed 30 mg. per hundred cubic centimeters in 78 of the cases and to be 50 mg. or more in 26 of these 78 cases. Thirteen, or 16.9 per cent, of the patients with a urea nitrogen content of the blood of 30 mg. or more died; 9, or 34.6 per cent, of those with an elevation of 50 mg. or more died, and 7, or 63.6 per cent, of those with an elevation of 70 mg. or more died. Among the 57 patients with a blood urea nitrogen con-

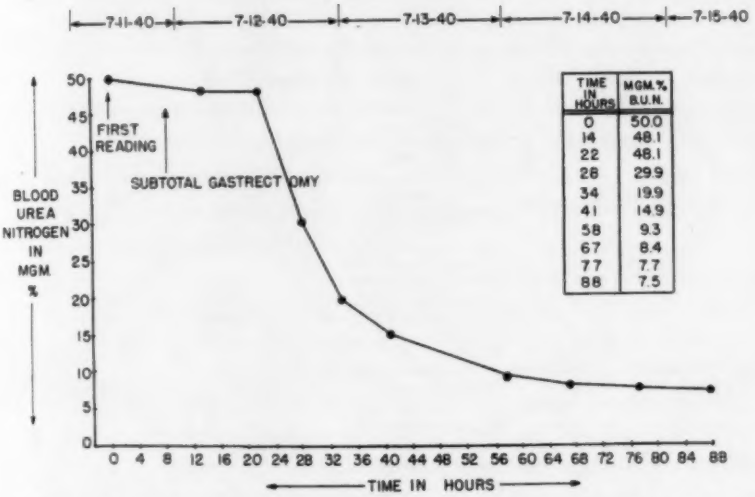

Chart 1.—Decline in the urea nitrogen level of the blood following gastric resection in a patient with bleeding peptic ulcer. B. U. N., urea nitrogen content of the blood.

tent of less than 30 mg. there were no deaths except 2 due to ruptured aortic aneurysm.

Our own data on this aspect of the subject are not extensive enough to lead to any conclusions. However, we wish to cite the case of a patient 49 years of age with bleeding of several days' duration. Because of the lack of improvement after being subjected to a conservative regimen and because of the high urea nitrogen content of the blood (chart 1) gastric resection was performed. The patient recovered. At operation a spurting branch of the pancreaticoduodenal artery was observed in the

14. Schiff, L.: Azotemia Following Hemorrhage, personal communication to the author, May 1940.

base of the ulcer. In another case, in which the patient died from postoperative bleeding after gastric resection, the urea nitrogen content of the blood ranged from 60 to 95 mg. per hundred cubic centimeters during the last five days of life. Holman [15] (1940) reported that in 2 of his 90 cases of bleeding peptic ulcer the urea nitrogen contents of the blood were high and rose until the time of death.

CAUSES OF AZOTEMIA

Numerous causes of azotemia accompanying hematemesis and melena have been considered by various authors (table 1). The most obvious classification of azotemia (and also of uremia) is according to renal and

TABLE 1.—*Factors Proposed by Various Authors as the Cause of the Rise in the Urea Nitrogen of the Blood Associated with Intraintestinal Hemorrhage*

Author	Date	Proposed Causes *
Sanguinetti	1934	Blood absorption, increased protein catabolism and chloropenia
Ingegno	1935	Blood absorption, hemorrhage, shock, dehydration and starvation
Meyler	1935	Dehydration, increased protein catabolism and blood absorption
Sučić	1935	Shock (producing decrease of renal function) and increased protein catabolism
Alsted	1936	Shock (producing decrease of renal function), dehydration, and blood absorption
Clausen	1936	Blood absorption
Borst	1938	Blood absorption and increased protein catabolism
Witts	1937	Blood absorption and decreased renal function due to shock
Crohn	1939	Shock
Schiff and co-workers	1939	Blood absorption
Kaump and Parsons	1940	Blood absorption and increased protein catabolism
Chunn and Harkins	1940	Blood absorption
Yuile and Hawkins	1941	Blood absorption

* The factor assigned the chief role is listed first.

extrarenal types. First consideration will therefore be given as to whether or not the azotemia under consideration is renal azotemia.

Renal Azotemia.—Sanguinetti [2] (1934), Christiansen [3a] (1935) and Ingegno (1935) found no evidence of renal impairment in their cases of hematemesis. Alsted [7b] (1936) observed a fall in the urea clearance to 15 per cent of normal in the presence of organically normal kidneys in a fatal case of hematemesis with a blood urea concentration of 216 mg. per hundred cubic centimeters.[16] He attributed the decrease of renal function to low blood pressure and diminished renal blood flow. In 4 other cases with less marked azotemia there was no reduction in renal

15. Holman, C. W.: Severe Hemorrhage in Gastric and in Duodenal Ulcer: A Study of Ninety Cases, Arch. Surg. **40**:150-160 (Jan.) 1940.

16. Alsted was one of many who expressed his results in urea rather than urea nitrogen as we have done. Since the values for the former are two and fourteen hundredths times those for the latter, the difference is appreciable.

clearance. Clausen (1936), Borst (1936 and 1938), Black [17] (1939) and Witts [11] (1937) all found decreased renal function in some of their cases.

The most extensive observations on this aspect of the question were those of Stevens, Schiff, Lublin and Garber [18] (1940). They concluded on the basis of their studies: "The reduction in the urea clearance may be due to the decreased renal blood flow but is insufficient to account for the increased blood urea content and persists in spite of the return of the blood urea nitrogen to normal. The elevation of the blood urea nitrogen content which follows hematemesis in the absence of shock is not due to impairment of kidney function." Johnson [19] (1940) observed no increase in blood urea nitrogen content in the absence of renal damage in patients who were fed blood by a stomach tube. However, Johnson did not state either the amounts of blood administered or the intervals afterward at which the determinations were made. Harris [20] (1940) stated that the rise of blood urea after hemorrhage is most likely due to the fall of blood pressure and probably has nothing to do with the hemorrhage as such. Lowered blood pressure in interfering with renal activity would cause accumulation of urea in the blood. Kaump and Parsons [21] (1940) stated: "From a study of the urea ratio values, we can probably eliminate renal failure as a factor."

It seems that any conclusions drawn cannot be applied to all clinical patients. Many patients have renal damage in addition to bleeding ulcer. In fact there are two reasons why patients with bleeding ulcer are especially prone to renal insufficiency: one of these is the possibility of renal damage from prolonged alkaline therapy; the second is that patients with arteriosclerosis—and hence possibly with renal insufficiency—are especially apt to continue bleeding once the latter begins. It is therefore impossible to state in each case that none of the azotemia is due to renal insufficiency.

An Experiment: Four experiments were performed on 2 dogs. Both these dogs had roentgen nephritis produced by the method of Hart-

17. Black, D. A. K.: Urea Clearance in Haematemesis, Lancet **1**:323-325 (Feb. 11) 1939.

18. Stevens, R. J.; Schiff, L.; Lublin, A., and Garber, E. S.: Renal Function and the Azotemia Following Hematemesis, J. Clin. Investigation **19**:233-237 (Jan.) 1940.

19. Johnson, J. B.: The Pathogenesis of Azotemia in Hemorrhage from the Upper Gastro-Intestinal Tract, J. Clin. Investigation **19**:776 (Sept.) 1940.

20. Harris, I.: Blood-Urea and Plasma Chloride in Experimental Haemorrhage, Lancet **2**:795-796 (Dec. 21) 1940.

21. Kaump, D. H., and Parsons, J. C.: Extrarenal Azotemia in Gastro-Intestinal Hemorrhage: I. General and Clinical Consideration, Am. J. Digest. Dis. **7**:189-190 (May) 1940.

man. In all experiments there was a rise in the urea nitrogen of the blood after the giving of blood by a stomach tube. This rise differed from that resulting in normal dogs only in that its duration was a matter of several days rather than of less than twenty-four hours. The degree of rise was no greater than in normal dogs.

Extrarenal Azotemia.—The whole question of extrarenal azotemia was reviewed by Wohl, Brust and Freed [22] (1938). They listed fifteen possible causes of extrarenal azotemia. It is becoming more and more recognized that azotemia often results from causes outside the kidney. Lemmer and Malec [23] (1939) reported an instance of extrarenal azotemia after drainage of the common duct. Adrenal insufficiency may produce azotemia. Swingle, Pfiffner, Vars and Parkins [24] (1934) stated that this syndrome "is probably extrarenal in origin." The liver also is closely bound up in the production of azotemia. Polack [10] (1936) expressed the opinion that toxic action on the liver played a role in causing azotemia after intraintestinal bleeding. As a prophylactic against this effect, he advised the injection of a solution of dextrose. Other factors that may be important in causing azotemia associated with bleeding peptic ulcer are as follows:

(*a*) Starvation: Schiff and Stevens [13] (1939) pointed out that since their patients were adequately fed, starvation could not be a factor. This likewise applies to most of the cases reported from Denmark by Alsted,[7] Christiansen [3] and others; the patients were treated by the Meulengracht diet.

(*b*) Dehydration: The role of dehydration was especially emphasized by Meyler [5b] (1936). He pointed out that in cases of gastric hemorrhage the output of urea is larger than may be accounted for by the absorption of lost blood; although part of it may be due to absorption, dehydration accounts for the rest. In a series of 53 instances of hematemesis or melena, Schiff and Stevens [13] (1939) observed that "as the level of urea nitrogen in the blood was frequently observed to rise during hospitalization in the presence of adequate administration of fluid it is believed that dehydration can be excluded as an essential factor in its increase." In our own experiments dogs given three subcutaneous injections of physiologic solution of sodium chloride daily and at the same time receiving blood by a stomach tube did not have such extensive azo-

22. Wohl, M. G.; Brust, R. W., and Freed, H.: Nonrenal Azotemia, J. Lab. & Clin. Med. **23**:450-458 (Feb.) 1938.

23. Lemmer, K. E., and Malec, J. P.: Drainage of the Common Bile Duct with Resultant Extrarenal Azotemia, Arch. Surg. **39**:125-130 (July) 1939.

24. Swingle, W. W.; Pfiffner, J. J.; Vars, H. M., and Parkins, W. M.: The Relation Between Blood Pressure, Blood Urea Nitrogen and Fluid Balance of the Adrenalectomized Dog, Am. J. Physiol. **108**:428-437 (May) 1934.

temia as dogs receiving blood alone, despite the fact that the latter were allowed to drink water freely. In all cases, however, definite azotemia resulted.

(*c*) Hemorrhage: Meyler [5a] (1935) and Vallery-Radot [25] produced azotemia in animals by repeated bleeding. Corbet [26] (1940) reported an unusual case of accidental hemorrhage in which the patient died of uremia. She was a woman aged 37 who was thirty weeks gravid. The bleeding was not severe, and since it was from the uterus to the outside, the possibility of absorption was slight. The experiments of Kaump and Parsons [27] (1940) are especially instructive. They showed that while hemorrhage will produce azotemia the elevation in blood urea nitrogen after the intragastric administration of blood to dogs is independent of hemorrhage.

(*d*) Anemia: Meyler [5a] (1935) stated that "the uraemia is not directly caused by anemia." Taylor and Lewis [28] (1915) demonstrated that anemia alone will not cause azotemia, and Schiff and Stevens [13] (1939) found no correlation between anemia and azotemia accompanying hematemesis or melena. Our own experimental results bear out this lack of correlation.

(*e*) Shock: Goldring [29] (1937) did not believe that absorption of lost blood can account for the increase of urea in the blood accompanying intestinal hemorrhage. Both he and Crohn [30] (1939) attributed the rise to shock. Schiff and Stevens [13] (1939) in their series of 53 cases of hematemesis or melena found that "elevation of the urea nitrogen content of the blood occurred in the absence of shock," and that "shock is not an essential factor in the elevation of the blood urea nitrogen which follows hematemesis."

(*f*) Hypochloremia: That hypochloremia and alkalosis accompanying protracted vomiting may be associated with azotemia is well known. A patient with a bleeding ulcer, however, seldom vomits more than once or twice. The relation between hypochloremia and azotemia has recently been studied by Kirsner and Palmer [31] (1941). They showed that administration of chlorides by mouth relieves azotemia associated with

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25. Vallery-Radot, P., cited by Christiansen.[3c]

26. Corbet, R. M.: Uraemia After Accidental Haemorrhage, Brit. M. J. **2**: 757-758 (Nov. 30) 1940.

27. Kaump, D. H., and Parsons, J. C.: Extrarenal Azotemia in Gastro-Intestinal Hemorrhage: II. Experimental Observations, Am. J. Digest. Dis. **7**: 191-194 (May) 1940.

28. Taylor, A. E., and Lewis, H. B.: A Study of the Protein Metabolism Under Conditions of Repeated Hemorrhage, J. Biol. Chem. **22**:71-75, 1915.

29. Goldring, W., in discussion on Christiansen.[3c]

30. Crohn, B. B., in discussion on Schiff and others.[35]

31. Kirsner, J. B., and Palmer, W. L.: The Rôle of Chlorides in Alkalosis Following the Administration of Calcium Carbonate, J. A. M. A. **116**:384-390 (Feb. 1) 1941.

alkalosis. They also pointed out, however, that hypochloremia can exist without accompanying azotemia; this had been noted previously by Kerpel-Fronius [32] (1936) and by Kirsner himself [33] (1941). Likewise, the investigations by Courriades [34] (1934) of experimental hypochloremia in dogs showed that hypochloremia is not necessarily accompanied by azotemia. It is of interest that Borst [8b] (1938) found hyperchloremia in association with azotemia in his cases. Kaump and Parsons [21] (1940) concluded from their clinical observations that "the blood chloride concentration per se has little to do with the elevation in blood urea" and from their experiments with animals they [27] concluded that "hypochloremia per se has nothing to do with the azotemia of gastro-intestinal hemorrhage."

(*g*) Increased Protein Catabolism: Increased protein catabolism was presented as an accessory factor by Meyler [5a] (1935), Sučić [6] (1935), Borst [8b] (1938) and Kaump and Parsons [21] (1940).

(*h*) Loss of Body Electrolytes: Wohl, Brust and Freed [22] (1938) considered the loss of body electrolytes an important factor.

(*i*) Absorption of Lost Blood: It is our belief that absorption of lost blood is one of the most important items in the production of azotemia accompanying intraintestinal hemorrhage. This does not mean that certain of the already listed mechanisms may not play an important role, but it is true that blood in the intestinal tract alone will produce marked azotemia.

MECHANISM OF THE PRODUCTION OF AZOTEMIA BY BLOOD IN THE INTESTINAL TRACT

The importance of blood in the intestinal tract in the causation of azotemia was recognized by Sanguinetti [1] (1933), the first worker on the subject, as well as by others (table 1). Sanguinetti [2] (1934) in his classic paper on the subject stated: "the increase of the blood urea was due in our cases to absorption from the intestinal tract of a considerable quantity of proteins." He also stated that an increase of protein catabolism and chloropenia played subsidiary roles. Schiff [14] (1940) stated: "It is felt that the digestion and absorption of the blood in the upper part of the digestive tract is the chief cause of elevation of the blood urea nitrogen."

Experimental Observations in Man.—Sanguinetti [2] (1934), Meyler [5b] (1936), and Schiff and co-workers [35] (1939) fed blood to patients, and

32. Kerpel-Fronius, E.: Salzmangelzustände und chloroprive Azotämie, Ergebn. d. inn. Med. u. Kinderh. **51**:623, 1936.

33. Kirsner, J. B.: The Production of Hypochloremia Without Azotemia, to be published.

34. Courriades, J., cited by Alsted.[7b]

35. Schiff, L.; Stevens, R. J.; Goodman, S.; Garber, E., and Lublin, A.: Observations on the Oral Administration of Citrated Blood in Man: I. The Effects on the Blood Urea Nitrogen, Am. J. Digest. Dis. **6**:597-602 (Nov.) 1939.

azotemia resulted. Sučić [6] (1935) and Clausen [9] (1936) made a similar experiment but obtained no elevation in the urea nitrogen level of the blood. At least in Sučić's case, this may have been because of too infrequent determinations. Christiansen [3c] (1937) gave 400 Gm. of veal to normal men in one dose. Only a slight postprandial rise of the urea in the blood occurred. The experiments of Schiff and associates [35] using both blood and meat so outnumbered those of all other experimenters combined and in addition were followed by so many more analyses of the blood, that there can be little doubt that feeding large amounts of blood or meat to normal persons will produce postprandial azotemia.

Experimental Observations in Animals.—Except for a few inconclusive experiments with rabbits by Sanguinetti [2] (1934), the first extensive series of experiments on the effect of feeding blood to animals was reported by Kaump and Parsons [27] (1940). Other animal experiments reported by Chunn and Harkins [36] (1940, 1941) and by Yuile and Hawkins [12] (1941) will be listed along with some original experiments.

(*a*) Effect of Whole Blood: A uniform rise in the urea nitrogen of the blood followed intragastric administration of whole blood to dogs.

(*b*) Effect of Intraperitoneal Injection of Blood: No azotemia occurred after intraperitoneal injection of blood.

(*c*) Effect of Iron: To rule out the action of the iron in the hemoglobin, 2 dogs were each given 1 Gm. of iron by a stomach tube in the form of 10 per cent iron ammonium citrate (1 Gm. of iron is the amount normally present in 1,000 cc. of blood). No azotemia resulted.

(*d*) Relative Effect of Cells and Plasma: In an attempt to find what element in the blood caused the rise, 5 dogs were given beef plasma by a stomach tube in the first series of experiments and in the second series of experiments 5 dogs were given beef cells in the same manner. In all 10 experiments blood samples were taken every day at 2 a. m., 8 a. m., 12 m., 4 p. m. and 8 p. m., one day before giving the substance to be tested and for at least two days afterward. In all instances the dogs given cells showed a much more marked elevation of the urea nitrogen level of the blood than did the plasma-fed dogs. A typical curve is shown in chart 2. That the cells rather than the plasma are the active principle in producing this type of azotemia was reported first by Chunn [37] (1940)

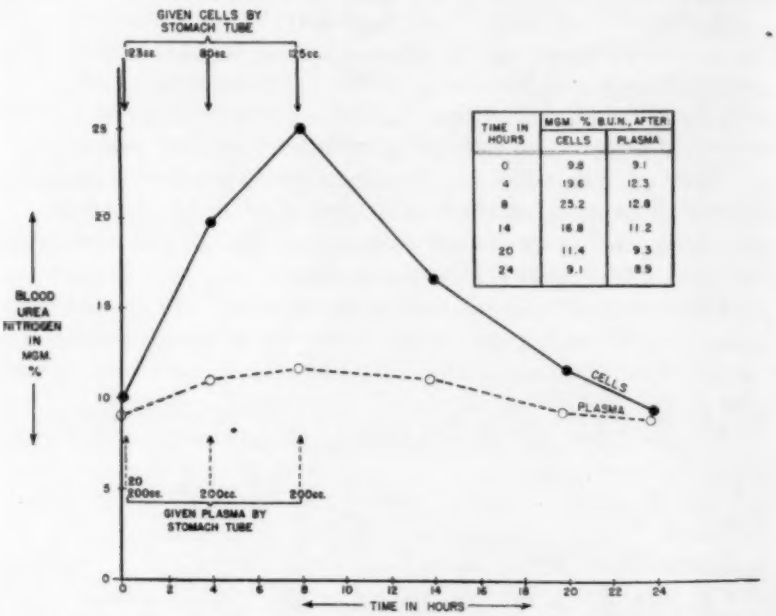
36. Chunn, C. F., and Harkins, H. N.: Alimentary Azotemia Due to Whole Blood Absorption from the Gastrointestinal Tract, Proc. Soc. Exper. Biol. & Med. **45**:569-571 (Nov.) 1940; Experimental Studies on Alimentary Azotemia: I. Rôle of Blood Absorption from the Gastrointestinal Tract, Surgery **9**:695-705 (May) 1941; Alimentary Azotemia: A Clinical Syndrome Occurring as a Part of the Bleeding Peptic Ulcer Complex, Am. J. M. Sc. **201**:745-749 (May) 1941.

37. Chunn, C. F.: Azotemia Following Intragastric Administration of Blood: Studies on Experimental Animals, Thesis, University of Michigan Graduate School, May 1940.

and later by Harkins [38] (1940) and by Boals, Chunn and Harkins [39] (1940). In a yet later paper, Yuile and Hawkins [12] (1941) reported independent data confirming this conclusion.

(*e*) Effect of Hemoglobin: Administration of a pure hemoglobin solution to 2 dogs produced a rise in blood urea nitrogen comparable to that produced by cells alone (table 2).

(*f*) Effect of Protein: Two dogs were given a single large protein meal consisting of casein and ground beef. The first dog received 83 Gm. of protein and the second 175 Gm. A marked rise in blood urea nitrogen occurred (table 3). That the protein in the cellular hemoglobin is the



TIME IN HOURS	MGM. % B.U.N., AFTER	
	CELLS	PLASMA
0	9.8	9.1
4	19.6	12.3
8	25.2	12.8
14	16.8	11.2
20	11.4	9.3
24	9.1	8.9

Chart 2.—Comparative effects of blood cells and blood plasma in the production of alimentary azotemia in dogs.

active element is corroborated by the results of Yuile and Hawkins [12] (1941). They showed in an excellent presentation that the rise in the urea nitrogen of the blood after the injection of various substances is quantitatively proportional to the protein content of these substances.

38. Harkins, H. N., in discussion on Schiff, L.; Stevens, R. J., and Moss, H. K.: Prognostic Significance of the Blood Urea Nitrogen Following Hematemesis and Melena, read at the Section on Gastroenterology of the American Medical Association, New York, June 12, 1940.

39. Boals, R. T.; Chunn, C. F., and Harkins, H. N.: Alimentary Azotemia: A Part of the Bleeding Peptic Ulcer Complex; Clinical and Experimental Studies, Program Meet. Cent. Soc. Clin. Research **13**:26, 1940.

(*g*) Effect of the Level in the Intestinal Tract at Which the Blood Is Given: The only observations on the effect of the level in the intestinal tract at which the blood is given prior to our own are those of Schiff and associates [35] (1939), who observed human beings. They fed blood into the fasting stomach through a Rehfuss tube and into the jejunum or the upper part of the ileum and the colon through a Miller-Abbott tube. The maximum increase in the blood urea nitrogen was greater when the blood was introduced into the jejunum or the upper part of the ileum. After injection of blood into the colon, no appreciable

TABLE 2.—*Effect of Hemoglobin in the Production of Alimentary Azotemia in Dogs*

	Blood Urea Nitrogen (Mg. per 100 Cc.) After Oral Administration of Hemoglobin	
Time (Hr.)	Dog 1 (60 Gm. Hemoglobin at 2 Hr.: 60 Gm. Hemoglobin at 6 Hr.)	Dog 2 (30 Gm. Hemoglobin at 2 Hr.: 30 Gm. Hemoglobin at 6 Hr.)
0	15.1	16.8
4	32.7	24.3
8	41.0	33.4
12	44.4	34.6
23	24.8	20.1
28	18.2	15.1

TABLE 3.—*Effect of Protein in the Production of Alimentary Azotemia in Dogs*

	Blood Urea Nitrogen (Mg. per 100 Cc.) After Oral Administration of Protein	
Time (Hr.)	Dog 1 (175 Gm. Protein at 3 Hr.)	Dog 2 (83 Gm. Protein at 3 Hr.)
0	15.6	16.3
4	23.4	17.3
8	42.0	34.1
14	40.9	29.4
20	21.0	20.3
24	14.9	16.5
28	11.6	15.9

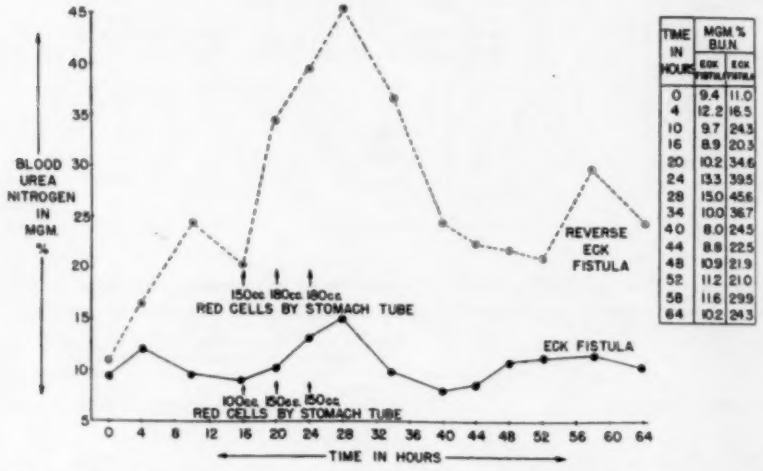
rise occurred. In clinical cases of bleeding into the colon, these authors observed no rise in the urea nitrogen of the blood. We performed 10 experiments on 4 dogs. Two of the dogs had jejunostomy of the Maydl [40] type 2 feet (61 cm.) below the ligament of Treitz, and the other 2 had an ileostomy of the Mann-Bollman [41] type 8 inches (20 cm.)

40. Maydl, cited by Markowitz, J.: Textbook of Experimental Surgery, Baltimore, William Wood & Company, 1937.

41. Mann, F. C., and Bollman, J. L.: A Method for Making a Satisfactory Fistula at Any Level of the Gastro-Intestinal Tract, Ann. Surg. **93**:794-797 (March) 1931.

proximal to the ileocecal valve. Blood or blood cells were introduced by a tube into the enterostomy openings. The effect of intrajejunal feeding was almost as marked as that of blood given by a stomach tube, while similar amounts of blood injected into the lower part of the ileum produced little effect. Azotemia seems to result, then, only from presence of blood in the upper intestinal tract.

(*h*) Role of the Liver: It is well known that the liver plays a major role in the formation of urea. In agreement with this is the clinical observation of Stadie and Van Slyke [42] that in cases of acute yellow atrophy of the liver, the blood urea values are low. Blood was given by tube in the usual manner to dogs with Eck fistulas and reverse Eck fistulas and after hepatectomy. In chart 3 it is shown that practically no



TIME IN HOURS	MGM % B.U.N. ECK FISTULA	MGM % B.U.N. ECK FISTULA
0	9.4	11.0
4	12.2	16.5
10	9.7	24.3
16	8.9	20.3
20	10.2	34.6
24	13.3	39.5
28	15.0	45.6
34	10.0	36.7
40	8.0	24.5
44	8.8	22.5
48	10.9	21.9
52	11.2	21.0
58	11.6	23.9
64	10.2	24.3

Chart 3.—Relative amount of alimentary azotemia after the injection of red blood cells into the dogs with Eck fistula and the dogs with reverse Eck fistula.

azotemia resulted in an animal with a typical Eck fistula, whereas the rise in the urea nitrogen of the blood in the animal with the reverse Eck fistula was actually greater than in the average animal with normal portal circulation. In chart 4 it is seen that despite the intraduodenal injection of blood into a liverless animal, the urea nitrogen level of the blood fell. It is of interest that the plasma prothrombin level fell at the same time.

ALIMENTARY AZOTEMIA—A PROPOSED NEW TERM

The name "azotemia" has been applied to this syndrome since the time of Sanguinetti's first description in 1933. The word "azotemia"

42. Stadie and Van Slyke, cited by Christiansen.[3c]

denotes the presence of urea or of other nitrogenous bodies in the blood in abnormal amounts. Arguing from analogy to the commonly used term "alimentary hyperglycemia," it seems logical that the urea syndrome be termed "alimentary azotemia." The mechanism in both is the same, and the adjective differentiates both conditions from similar ones of different causation. Use of the designation "extrarenal azotemia" is not definitive enough. "Alimentary azotemia" means the azotemia due to ingestion of excessive proteins. In bleeding peptic ulcer it is probable that a large share of the resultant azotemia is alimentary azotemia due to ingestion of blood proteins; part of it may be due to other types of extrarenal azotemia, while in some instances actual renal azotemia may be a contributory factor.

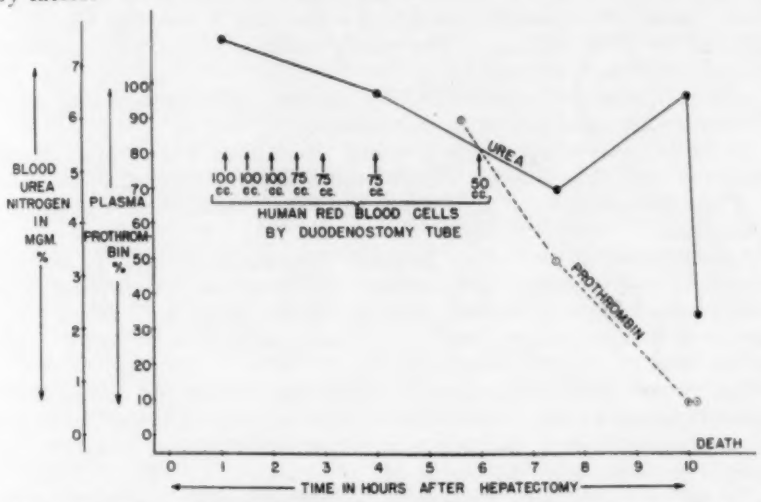


Chart 4.—Effects of the administration of red blood cells on the urea nitrogen content of the blood and the plasma prothrombin level after total hepatectomy.

CONCLUSIONS AND SUMMARY

Alimentary azotemia occurs in cases of massive hemorrhage into the upper intestinal tract, a common example of which is bleeding peptic ulcer.

The degree of azotemia is of considerable prognostic significance; high blood urea nitrogen values are associated with a high mortality rate. Persistent azotemia tends to indicate persistent bleeding in most instances rather than serious hepatic or renal damage, and therapeutic indications are calculated accordingly.

In cases of hematemesis and melena, azotemia is essentially caused by absorption of the red cells rather than of the plasma fraction of the lost blood. This is accounted for by the high protein content of the cell hemoglobin.

In our experiments starvation, dehydration, bleeding, anemia and shock did not play a major part in the production of azotemia.

Presence of the liver with an intact portal circulation is essential for the occurrence of alimentary azotemia.

The term "alimentary azotemia" is proposed for the syndrome of increased blood urea nitrogen following alimentary absorption of large amounts of digested protein. This condition occurs clinically most often in patients with bleeding peptic ulcer.

ABSTRACT OF DISCUSSION

Dr. D. H. Kaump, Detroit: Parsons and I have shown that the rise in blood urea is dependent to a large extent on the amount of blood given to the experimental animal. It is therefore logical to assume that a continued rise in urea values of the blood indicates a continuously bleeding process and consequently presages the death of the patient.

Repeated estimations of blood urea for patients with bleeding syndromes are of vastly greater value than single determinations.

As to the cause of alimentary azotemia, Parsons and I were unable to find evidence of renal failure in our experimental animals. However, in the human being with damaged kidneys, one might expect a slight acceleration or prolongation in this rise.

I doubt whether shock is of any particular consequence in relation to alimentary azotemia because in patients with bleeding peptic ulcers the shock element is not as great as one might expect from the degree of urea rise. With adequate treatment, the urea values fall to normal but much more slowly than the patient recovers from shock.

Drs. Harkins, Chunn and Boals observed a less marked urea rise in animals adequately hydrated by the administration of physiologic solution of sodium chloride and of dextrose; that is equally true in human beings because in patients with alimentary azotemia there is a prompt fall in the urea values with the administration of fluids. Consequently, dehydration probably does play some part. I doubt whether the sodium chloride in the fluids contributes much to this recovery, primarily because the urea values fall to normal long before the blood and urinary chlorides reach normal levels.

Dr. Leon Schiff, Cincinnati: This work is particularly gratifying as it confirms a number of observations made by my associates and me in human beings.

While a number of factors, particularly renal, may play a role in the causation of azotemia in a given patient with hematemesis or melena, the essential factor is the presence of blood in the upper intestinal tract. Everything else being equal, the degree of azotemia is dependent on the amount of this blood and the unit of time in which it appears.

The evidence in one of the experiments convinced my associates and me that it was the digestion of the blood protein in the intestinal tract and the absorption of these digestive products which accounted for the azotemia in question.

Azotemia which follows hematemesis in patients with hepatic cirrhosis is of even greater prognostic import than that seen in patients with bleeding peptic ulcer; that which occurs in the presence of obvious nephritis is of less import. Over half the patients who have come to my notice with bleeding esophageal varices and with a concentration of urea nitrogen in the blood of 30 mg. per

hundred cubic centimeters or more have died shortly after the onset of hemorrhage. This may be explained by the fact that the degree of azotemia was not a true expression of the extent of the loss of blood because the liver's ability to produce urea nitrogen was impaired. When nephritis is present the degree of azotemia may be exaggerated as the result of impaired kidney function.

Occasionally there is no azotemia after severe hematemesis, even within a day or two after hemorrhage. This may be explained by (1) external loss of most of the blood through vomiting, (2) intestinal hypermotility, sometimes induced by a cathartic taken immediately after hematemesis (as occurred in 2 of our cases), (3) renal excretion of urea exceeding the production of urea and (4) factors as yet unknown.

Dr. Walter L. Palmer, Chicago: The authors are to be congratulated on devising the appropriate term "alimentary azotemia."

They and others have shown the preeminent role of increased blood in the intestine as a cause of alimentary azotemia. A priori, one would think that renal function would play a considerable role in causing the elevation of the level of the urea nitrogen of the blood. When the blood pressure suddenly drops from 140 or 130 to 90 or 80, one would think there might be sufficient decrease in the renal blood flow to bring about significant reduction in renal function. However, this does not seem to happen; the present authors and other workers have shown that normal or almost normal renal function is present under such circumstances. In the last 2 patients whom I have seen with massive hemorrhage from peptic ulcer and marked increase of the blood urea nitrogen the urea clearance test of renal function yielded results within normal limits.

The prognostic value of the elevated level of the urea nitrogen of the blood does seem to be definitely established. In the 1 case that has come to my attention in the last year or two in which a patient died the patient had the highest blood urea nitrogen I can recall having seen. Of course, the essential thing in cases of massive hemorrhage is not the amount of blood in the intestine but the amount of blood left in the cardiovascular system. The physician should be able by means of continued or frequent blood transfusions to compensate for the blood lost in the intestines and in some way or other bring about cessation of the hemorrhage and eventual recovery. However, this does not seem always to be possible. The elevation of the level of the blood urea nitrogen is helpful in enabling us to estimate the amount of blood lost.

Dr. Henry N. Harkins, Detroit: I agree that persistent elevation of the level of the urea nitrogen of the blood indicates persistent bleeding. It should be emphasized that conclusions drawn from any experimental work have to be applied to human beings with caution, because in human beings other factors may be of importance. There are two reasons why human patients are apt to have complicating conditions more often than dogs. First, patients who have peptic ulcer with persistent bleeding are apt also to have arteriosclerosis. In fact, these patients have arteriosclerosis in a higher proportion than the average population. That is why the ulcer tends to continue bleeding. Second, many patients with peptic ulcer have been treated with alkalis over a long period, and this may have impaired their renal function to some extent.

There was not time to mention that Dr. Schiff and co-workers were the first to point out that the intestinal level of bleeding was of importance, but the findings in our experiments with animals agree with their data from patients that only blood in the upper intestinal tract will cause this increase in the urea nitrogen of the blood.

However, if urea itself is put into the intestine at two levels, the urea nitrogen becomes increased in both instances. This indicates that the urea is absorbed at both levels. Why absorption of blood low down in the intestinal tract does not cause a rise in the urea nitrogen is not explainable at present.

I believe that among others Dr. M. G. Wohl once said that this syndrome cannot be due to absorption, because the phenomenon does not occur in cases of ectopic pregnancy. My associates and I have placed blood within the peritoneum in animals and have observed that the urea nitrogen of the blood did not increase. It is probable that even if the blood is absorbed from the peritoneal cavity, the absorption is so slow in comparison with that which occurs from the intestine that no azotemia results.

Dr. Schiff, Dr. Kaump and others have emphasized the importance of frequent readings both for experimental animals and for patients. In many previous observations these elevations have been missed because the readings were not frequent enough. I can vouch for the importance of frequent determinations from personal experience, because in our experiments Dr. Chunn and I had to obtain readings at all different hours of the night; in fact, since the animals were usually fed in the daytime, the night readings were those which showed the highest elevation.

There has been a prejudice against surgical intervention in cases in which the urea nitrogen level of the blood is elevated. I think the work presented emphasizes that this may not always be logical and that actually the presence of a rise in the urea nitrogen of the blood may be an indication for operation, other things being equal, rather than a contraindication.

HYDATID DISEASE (HYDATIDOSIS)

HYDATID CYST OF THE LUNG

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After the liver the lung is the most frequent site of the localization of hydatid cysts. Those hexacanth embryos which are able to pass through the hepatic filter cross the right side of the heart and reach their second filter, the lung; here they can attach themselves and develop into hydatid cysts.

Hydatid cysts of the lung can be central or peripheric. The latter, through their ever increasing growth, can come into contact with the pleura. Whether central or peripheric, a pulmonary hydatid cyst may empty into a bronchus and be expelled through a hydatid vomica.

Sometimes, when the entire parasite (fluid and membranes) is expelled, spontaneous healing of the disease occurs. If only the fluid is eliminated, the membranes will remain in the adventitial cavity where the retraction of the cavity's walls and the narrowness of the bronchial opening make the expulsion of the membrane almost impossible (incarcerated membrane).

In contrast with the adventitia of a cyst of the liver, that of a cyst of the lung has only two layers: the inner stratum, thin and composed of connective tissue, and a thicker outer one, formed by atelectatic lung tissue which has recuperative powers (false adventitia).

From the clinical point of view, the hydatid cysts of the lung may be divided into ordinary and complicated cysts.

The former are always latent and offer no symptoms. Sometimes there is a slight dry cough with slight hemoptysis; pain is exceptional, unless the cyst is in contact with the pleura. In any case, a cough, slight hemoptysis and pain may suggest the presence of a disorder of the lung but never point to any definite diagnosis.

If there is a cyst of the lung, a roentgen examination of the thorax, indispensable even in the briefest clinical examination of this region, shows a more or less rounded shadow. However, it must be borne

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This is the third article on hydatid disease contributed by Dr. Arce at the sugestion of the Chief Editor of the ARCHIVES.

in mind that this shadow, even if the patient has pain, cough and hemoptysis, will never uphold a positive diagnosis.

The signs and symptoms just stated, a good general condition and a positive biologic syndrome (eosinophilia, with the Imaz-Lorentz complement fixation test and the Casoni test of the skin both positive) can secure a probable diagnosis but never an absolute one. The only absolute

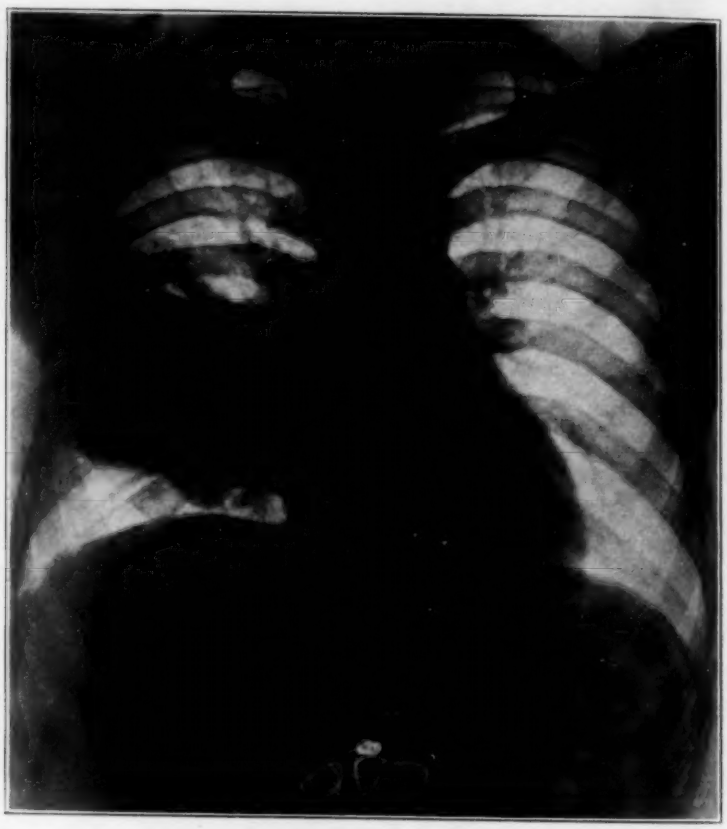

Fig. 1.—Roentgen image of the perivesicular pneuma.

sign is a hydatid vomica (hydatidophthysis) with hydatid membranes, scolices or hooks in the expectorated matter.

On the other hand, complicated hydatid cysts offer positive signs for an absolute diagnosis. As the complications originate in the sphere of the bronchi, it is convenient to stress here the importance of the process by which the cysts open into the bronchi and describe the different degrees to which this takes place.

The bronchial wall having been gnawed by the eccentric growth of the parasite, the outer aspect of the latter comes into contact with the

lumen of the bronchus. One or more deep breaths or fits of coughing may bring a small amount of air in between the parasite's membrane and its adventitia. This can be detected by means of roentgenograms; the air appears in the shape of a cap and gives rise to what is called the "perivesicular pneuma" (fig. 1). This typical roentgen picture allows a definite and absolute diagnosis.

At a later stage, the membrane is torn, and part of the fluid is expelled and replaced by air. The latter finds its way in between the

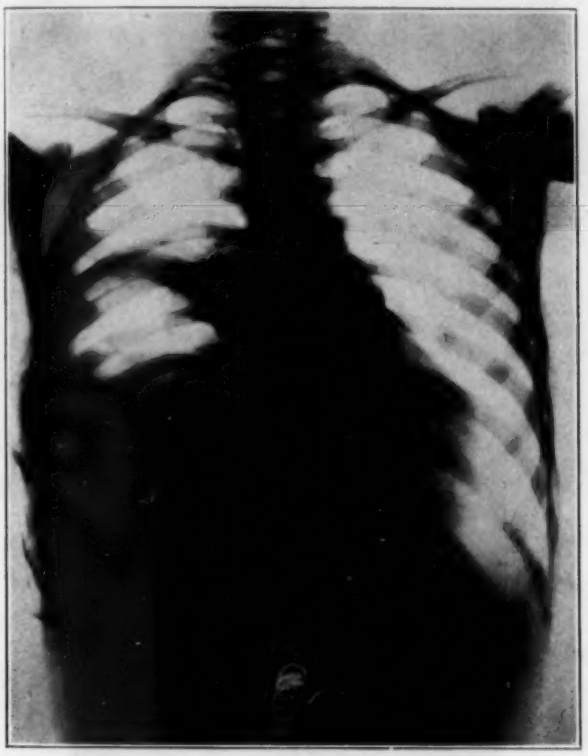

Fig. 2.—Roentgen image of the double arch.

adventitia and the membrane and also between the membrane and the remaining fluid. On roentgen examination, the membrane shows two air chambers, the upper one in contact with the adventitia and the lower one in contact with the fluid level. This is the "double arch image," described by my co-worker Prof. Oscar Ivanissevich (fig. 2).

The cystic membrane may become torn or totally disintegrated, and the whole or just part of it may float on the remaining fluid. The roentgenographic image shows an air cap on the upper section and a dull, movable and horizontal shadow on the lower (the hydatid fluid).

Between the two a lighter shadow can be seen; it is the cystic membrane or one of its fragments floating like a water flower on the fluid. It is the "water flower sign" (fig. 3).

To form the pictures just described, the presence of a part or the whole of the hydatid fluid is absolutely necessary. However, it may

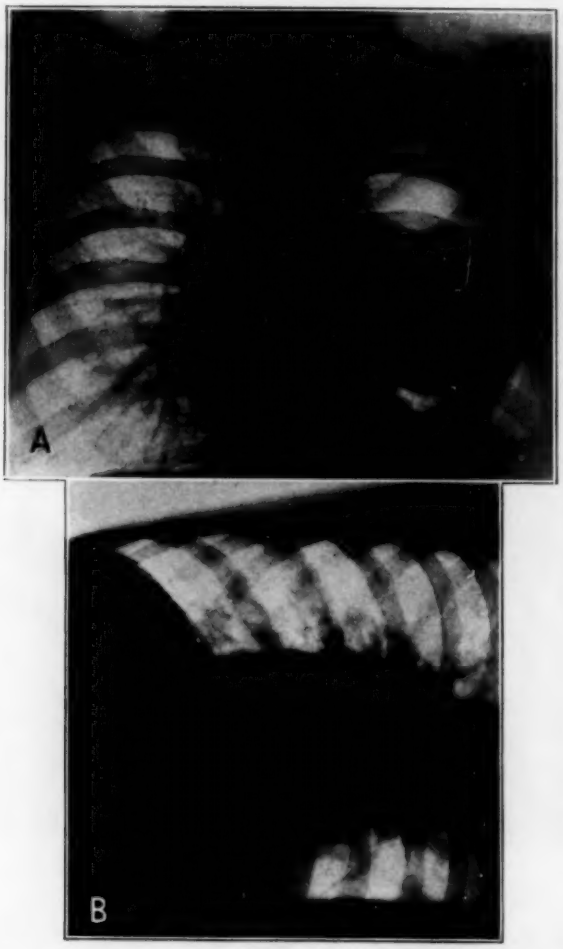

Fig. 3.—*A*, Roentgen image of the water flower taken from a standing position; *B*, from a recumbent sign position.

happen that all of it has been expelled and only the membrane remains. This is what I called before an incarcerated membrane. The frontal roentgenographic image of this is almost circular (though obviously it will be less opaque than the image of an uncomplicated hydatid cyst), but the lateral one is polygonal (fig. 4). The contrast between the two

images may be due to the uniform retractibility of the membrane in the frontal direction (round frontal image) but rather difficult retractibility in the anteroposterior direction on account of the membrane's connections with the bronchi (it must be remembered that the bronchial divisions take place only in the anteroposterior direction). Although these reasons are not absolute, the fact remains that the concomitance of both images in a patient allows a positive clinical diagnosis.

The surgical treatment of hydatid cyst of the lung consists of two operative stages, thoracotomy and treatment of the cyst.

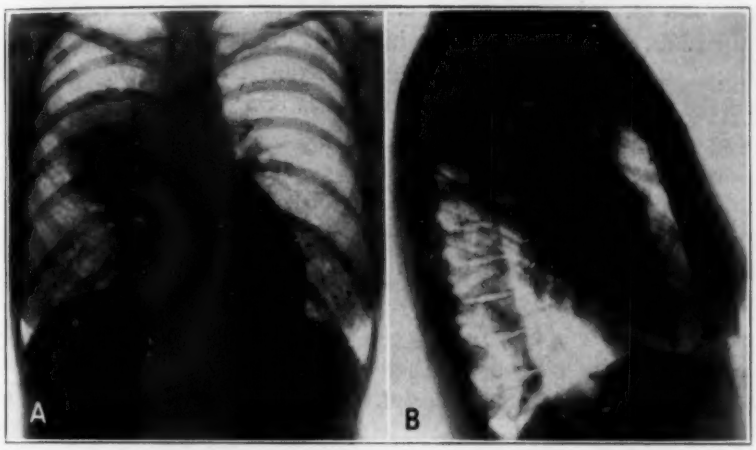

Fig. 4.—*A*, frontal roentgen image of an incarcerated membrane, showing the circular borders; *B*, lateral image, showing the polygonal borders.

TECHNIC OF TREATMENT

A. *Thoracotomy.*—The opening of the thorax differs according to the presence or absence of pleural adhesions.

1. If confirmed adhesions have placed the lung in contact with the thoracic wall at the level of the cyst, the operation becomes a simple one. Under local anesthesia, 10 cm. of the lowest rib situated within the zone of the adhesions is resected. Once the pleura is exposed, the cyst is opened (pleuropneumonotomy) and its contents removed.

However, the surgeon should never trust that all adhesions are sufficiently numerous and solid to allow this easy operation. It is therefore advisable to proceed with the utmost care once the rib has been removed.

First of all, the surgeon should determine whether the lung slides under the parietal pleura or not. If there are no adhesions, this motion can be easily elicited by asking the patient to breathe in deeply.

If the lung is not seen to move or even if a process of adhesive pleuritis in the exposed zone is observed, the surgeon should go slowly, layer by layer, until he is certain he has reached the lung tissue. If there are no adhesions present and the parietal pleura has been cut, the shiny inner pleural layer (visceral pleura) can be clearly seen forming an independent structure, even when no air goes in and the lung does not become retracted. This may occur in cases in which there is a normal pleura, cases in which large cysts are in contact with the thoracic wall or in which there are only loose adhesions.

If pleural adhesions are present, the roentgen examination, which should be carried out by the surgeon himself in all cases of thoracic disturbance, will show the zone in which the operation should be performed. If there are lateral adhesions, the shadow comes in contact with the thoracic wall when the patient is examined from the front or from the back; this situation calls for lateral thoracotomy between both axillary lines. If there are frontal or posterior adhesions, the shadow comes in contact with the thorax in the front or back only when the patient is examined in profile or in oblique positions. Such a picture indicates either anterior or posterior thoracotomy, according to the type of adhesions.

In short, there is only one way of making absolutely certain whether or not there are adhesions, and that is by producing an artificial pneumothorax. This method is also useful when the roentgenogram shows one or more unreliable shadows, as it will clarify the diagnosis. If the contact between the lung and the thorax persists in spite of the production of a pneumothorax carried out at high positive pleural pressures, there is no doubt whatever about the presence of adhesions.

I have already spoken about the great care that should be taken before operation to avoid being met with an absence of adhesions or the presence of small or loose ones. If one arrives at this pass, what is to be done? Personally, when I am going to operate with use of a local anesthetic, I have the patient placed under a closed circuit anesthetic apparatus, which is made to work with oxygen alone when the need arrives. Moderate pressure on the oxygen-containing elastic bag is enough to increase the pressure inside the lung and thus bring both pleural layers together. The operation is performed as if the patient were under inhalation anesthesia with hyperpressure *(baronarcose)*.

In the absence of a closed circuit anesthetic apparatus, it is better to fix the lung to the thoracic wall before opening the pleura. This is done with two or more stitches (harpooning) which cross the soft structures of both the costal wall and the lung. The stitches should be

placed well outside the zone in which the cyst is supposed to be, so as to prevent the needle opening the cyst before it is time to do so.

Of the foregoing two procedures, my preference lies with the first.

Once the cyst has been opened and its contents removed, if there are no adhesions or if those present are found unsatisfactory, the edges of the adventitia are attached to those of the structures under the skin. This is carried out by means of loose stitches, preferably crossing the intercostal muscles or, in defect of these, the deepest muscular layer of the thoracic wall.

Adhesions are the rule, or at least occur frequently, in connection with complicated cysts, particularly those which have become septic to the point of being true hydatid abscesses. These adhesions, sequelae of the pulmonary and pleural inflammation caused by infection of the cyst's neighboring structures, lead to the formation of a pleural symphysis. This fortunate defensive process allows the performance of pneumonotomy and evacuation of the cyst's contents by a simple operation.

2. In the absence of adhesions, four procedures can be carried out: (*a*) the creation of artificial adhesions; (*b*) the production of pulmonary hyperpressure with or without inhalation anesthesia; (*c*) the harpooning method according to Posadas' technic; (*d*) the preoperative production of an artificial pneumothorax (Arce's method).

The first three maintain the contact between the lung and the thoracic wall to avoid a pneumothorax; the last method, on the contrary, causes a pneumothorax to be present.

(*a*) The method of creating artificial adhesions (sometimes called the method of Lamas and Mondino, after the two Uruguayan surgeons who devised it) consists in localizing the cyst in detail by roentgenographic, tomographic, and other methods, removing 4 to 6 inches (10 to 15 cm.) of the rib nearest the tumor and packing the wound with plain or iodoform gauze. The packing, through compression and irritation of the zone of the pleural membranes above the site of the tumor, gives rise to a process of plastic adhesive pleuritis. The packing is changed if necessary once or oftener, and after two weeks (sometimes three) strong adhesions will have been formed. These will enable the surgeon to open and empty the cyst without risk of the development of an operative pneumothorax or of contamination of the pleural cavity.

(*b*) The method of pulmonary hyperpressure may or may not be combined with inhalation anesthesia (*baronarcose*). It requires the application over the patient's face of an apparatus which will allow the closing of the respiratory circuit and the increase of the gases contained therein. With hyperpressure ranging between 2 and 7 mm. of mercury, the pleura can be opened and the lung exposed without fear that the latter may become retracted as in those cases in which the pleural cavity is opened in the absence of adhesions.

Compared with the first, this method offers the advantage of allowing exploration of the lung and exact localization of the cyst. All exploratory procedures must be carried out with a small degree of hyperpressure, so that the surgeon may introduce his hand into the pleural cavity and feel the lung until the cyst is localized exactly. Then the part of the lung containing the cyst is drawn to the operative wound. The hyperpressure is increased at this moment so as to establish an intimate contact between both pleural membranes, thus avoiding the possibility of blood or cystic contents entering the pleural cavity when the cyst is opened.

(*c*) My teacher Posadas first published a description of his harpooning method in 1898. An osteomusculocutaneous flap containing two ribs is made over the site where the cyst has been localized by roentgen examination. (This localization should be carried out with the utmost care so that perforation of the cyst may be avoided at the next stage.) Once the parietal pleura has been exposed, both pleural membranes and the lung are united by two untied loose stitches of thick catgut (made with a Hagedorn needle). These stitches, situated above and below the cyst, penetrate the lung tissue and afterward leave it at a certain distance from the point of penetration. The loose ends of the catgut are maintained tense to keep the lung well in contact with the costal wall, thus avoiding the formation of a sudden pneumothorax at the moment of the pneumonotomy and evacuation of the cyst.

This method can be connected with the operative pneumothorax because, though Posadas carried it out in order to avoid the effects of a pneumothorax, it is impossible to avoid with it a slight tearing of the parietal pleura and consequent penetration of some air into the pleural cavity with the formation of a small operative pneumothorax.

Other surgeons pay no heed to this preliminary harpooning method. They simply open the parietal pleura and allow air to penetrate in a slow way (slow operative pneumothorax of the French school). Later, with the hand or instruments they draw the pulmonary lobe wherein the cyst lies to the operative wound and finally perform the pneumonotomy and evacuation of the cyst.

(*d*) Since I propounded the method of preliminary pneumothorax in 1919,[1] I use it exclusively. The technic of this method is described in an article of mine on thoracotomy with free pleura, published in 1926.[2] The preliminary pneumothorax produces atelectasis of the lung to the point that this organ becomes retracted around the cyst and against the hilus. On account of this retraction, it is better to reach

1. Arce, J.: Preliminary Pneumothorax in Lung Surgery, Surg., Gynec. & Obst. **36**:687 (May) 1923.

2. Arce, J.: The Technique of Thoracotomy with Free Pleura, Surg., Gynec. & Obst. **33**:355 (Sept.) 1926.

the cyst through a more or less high anterior thoracotomy (in the region of the second to the sixth rib, according to the site of the cyst). Yet it happens sometimes that either the cyst or the lung has become partly adherent to the costal wall (axillary zone or posterior zone) so that the pneumothorax does not give rise to the total retraction of the lung. In such a case it is advisable to perform the thoracotomy according to the information provided by the roentgen examination, which the surgeon should carry out personally the day before the operation.

Once the pleura is opened, the surgeon explores the hemithorax, localizes the cyst or cysts and with his hand draws the parasite-infected lobe to the operative wound for the performance of the pneumonotomy and evacuation of the cyst. The lung should be treated gently, and any pulling ought to be done with the utmost care, in order not to diminish the advantages offered by the preliminary pneumothorax. It is therefore wise to avoid the use of instruments when drawing the tumor to the operative wound. The bare hand will not injure the lung tissue, and any reflexes provoked will be at a minimum.

It has been stated, purely from a theoretic standpoint, that a preliminary pneumothorax handicaps traction of the tumor toward the operative wound. My wide experience in this connection has taught me that such is not the case. If, owing to adhesions, the lung has not become totally retracted and the surgeon endeavors to draw it to the opposite side because of a faulty thoracotomy incision, it is perfectly obvious that he will find this task most difficult. Yet it must be borne in mind that although as a rule this method calls for an anterior incision, there are, as I have already stated, exceptions which can and must be foreseen by a simple roentgen examination. This examination must be carried out by the surgeon himself on the day before the operation. If there are still any doubts, a tomographic examination will definitely clear the picture.

B. *Treatment of the Cyst.*—Whenever possible, it is well to protect the pleural cavity before opening the lung. This should be done throughout the wound by means of sterile gauze towels soaked in warm solution of sodium chloride. This measure is indispensable when the operation is performed under hyperpressure or with a preliminary pneumothorax.

1. How should the cyst be opened? The first step is to make an exploratory puncture for the purpose of verifying the diagnosis. Complicated cysts and those which have emptied themselves into a bronchus give no response to this procedure, a fact which is of no importance when the patient's clinical record is borne in mind. The introduction of the needle into the lung and its contact with the pathologic process provide a peculiar tactile sensation which is easier to perceive than to describe and is totally different from that in the case of a solid tumor.

If the puncture gives origin to a flow of clear fluid, this should be drawn out gently and slowly, the syringe being changed as often as necessary. During this procedure, the point of the needle remains in the cavity of the cyst, while the outer part is plugged by an assistant every time a syringe full of fluid is withdrawn. In order to avoid having to change the syringe more than once or twice, I usually replace the one used for exploratory purposes by another with a capacity of 100 cc.

I advocate the gentle and slow method of drawing out the fluid. Finochietto propounds instead the abrupt and rapid drawing out of the fluid by means of a trocar attached to a flask in which a vacuum has previously been made. I use this procedure in operating on a cyst of the liver and large cysts of other organs but never in operating on a cyst of the lung. I am firmly convinced that the abrupt method offers certain inconveniences which do not arise with the slow and gentle one.

When the cyst has been totally emptied, the needle is removed and in its place an incision (pneumonotomy) is made. This incision should not be too long but should reach the cavity of the cyst. Then the edges of this incision are held open while the surgeon, with a flexible clamp or a heart forceps, removes the hydatid membrane and ends this stage by drawing off any remaining fluid with gauze swabs. All these steps should be carried out as gently as possible, particularly when operating with only the field under anesthesia. In this case the contact of the swabs (or of any foreign body, for that matter) with the small bronchi open on the adventitial membrane gives rise to fits of coughing and other disturbances in the patient. I have made a habit of using the speculum procedure after the fashion described in discussing cysts of the liver when inspecting and cleaning the walls of the cavity of medium-sized and large cysts.

When I am faced with an incarcerated membrane after having both observed an absence of fluid by means of the exploratory puncture and performed the pneumonotomy, I remove the membrane, which is in a varied condition of disintegration, and cleanse the cavity thoroughly.

In operating on hydatid abscess, it is best to withdraw the contents with a needle of large diameter or with the smallest trocar of the electric suction apparatus. When the latter is employed, care should be taken to have only enough pressure to run the pus into the suction flask. These precautions, together with the protecting towels soaked in warm solution of sodium chloride, will undoubtedly preserve the pleural cavity from contamination. Once the suction process is over, the pneumonotomy and the cleansing of the cavity are carried out as in the other cases.

2. What is to be done with the adventitial cavity after the parasite has been removed and the cavity cleansed? The adventitial pouch of septic cysts and, generally speaking, of all complicated cysts must be marsupialized and drained. This is done by suturing the edges of the incision in the lung to those of the operative wound. This suture includes not only the parietal pleura but also the intercostal muscles and the endothoracic fascia; this provides the marsupialization with greater support and strength. If these structures are found to be weak, the surgeon should not hesitate to include in the suture the deepest layers of the thoracic muscles.

If the cyst is aseptic, Posadas' method, that is, suture without drainage, may be employed, but I perform it only in cases in which there are small or multiple cysts. Experience has taught me that although marsupialization of a cyst of the lung does not offer the same inconveniences as that of a cyst of the liver, the closing without drainage may engender some difficulties. These usually are due to the opening of one or more small bronchi into the adventitial pouch; this may give rise to an infection which may and often does develop into a true post-operative abscess of the lung.

In a case in which there was a conglomeration of cysts in a lingula of the anterior border of the right lung, I partly resected this lingula. This case was undoubtedly exceptional, but under similar circumstances there should be no objection to a lobectomy, especially if the entire lobe or the greater part of it is affected by the disease.

HYDATID CYST OF THE KIDNEY

The elimination through the urine of daughter vesicles, proliferous vesicles, scolices or hooks definitely confirms the diagnosis in those cases in which a hydatid cyst of the kidney is suspected.

In all other cases a positive diagnosis is impossible, but with a good general condition, a hydatid cyst of the kidney might be suspected before a tumor of long evolution. This possibility may be further strengthened by a positive biologic syndrome.

If the tumor protrudes in the renal pelvis, the groove which appears in the pyelogram usually takes the shape of a segment of a sphere.

In the great majority of cases, the diagnosis is made on the operating table.

The long evolution of the hydatid cyst of the kidney, together with the fact that it has no bearing on the patient's general condition, explains why this disease in the great majority of cases is discovered only when the greater part of the organ has already been destroyed. Then there is no alternative but to perform a nephrectomy.

Yet sometimes the surgeon finds small or medium-sized cysts which have not affected the entire organ. If these are localized on the lower

end of the kidney and do not interfere with the renal pelvis, their total removal is possible by a partial resection in the shape of a triangle, thus avoiding a total nephrectomy. Of 13 cases observed at the clinic of the Surgical Institute it was possible to use this procedure in only 1.

A cyst of the kidney should never be marsupialized. This technic should be avoided, unless it is absolutely indispensable because of indications of a general character, such as the condition of the patient or that of the other kidney.

HYDATID CYST OF THE SPLEEN

Hydatid cyst of the spleen is even more difficult to diagnose than that of the kidney. Only the increase in size of the organ or the presence of a large tumor in the left hypochondrium of a patient coming from a zone of infection may suggest the disease.

The best treatment for the splenic cyst is splenectomy. Marsupialization is usually followed by long-standing fistula, which leads to amyloid degeneration of the spleen and later to that of the liver and kidneys.

HYDATID CYST OF THE BRAIN

It is almost impossible to diagnose hydatid cyst of the brain. Obviously, the clinical signs derived from irritation or compression of a zone containing important functional centers may lead to the diagnosis of a tumor of the brain but will never point out its parasitic nature. If the cyst lies in a silent zone, it may reach a great size without showing any outward signs except for the general ones of cranial hypertension in the late stages. At any rate, a ventriculogram will generally allow exact localization of the tumor and point out the only possible therapeutic course, surgical intervention.

In children the hydatid cyst is often seen to come into contact with the endocranium. It is often the cause of wasting and thinning of the bones of the vault, which can sometimes be felt with the fingers and gives a sensation of parchment (parchment sensation).

The operation consists of an exploratory craniotomy and exposure of the affected zone of the brain. If the tumor has reached the cortex, the adventitia is cut at an avascular point and the hydatid punctured. After the fluid has been evacuated, the germinative membrane is carefully extracted through the hole in the adventitia, pains being taken that it is not torn or fragmented lest any fluid fall on the operative field.

All these procedures should be carried out with the utmost care, as the adventitia is so thin that some authors have even denied its existence. It is formed by scanty connective tissue from the vessels and by neuroglial elements and therefore these appear in the form of a veil-like membrane surrounding the hydatid cyst.

The operation ends with the suture of the dura mater and the replacement of the flap of scalp and bone, without leaving drainage.

If the tumor does not appear on the surface of the brain, it must be discovered by an exploratory puncture followed by suction of all the hydatid fluid. A small incision on the cortex will later permit removal of the parasitic membrane.

SECONDARY HYDATIDOSIS

The formation of hydatid cysts may be due to other causes than ova of Taenia echinococcus in the intestine of man. Scolices contained in a ruptured human hydatid cyst may attach themselves in any part of the human body and give rise to cysts identical with those from which they came. This process is called secondary hydatidosis. If the ruptured cyst empties its contents into a blood vessel, the blood stream carries the scolices to the organ to which they become attached. This gives origin to what is called metastatic secondary hydatidosis.

The most frequently occurring form of direct secondary hydatidosis, that without intervention of the blood stream, is peritoneal hydatidosis. The frequency is easily understood if it is remembered that in 70 per cent of the cases hydatid cysts occur in the liver and that the surface of this organ in contact with the peritoneum is indeed large. Besides, clinical and pathologic figures show that rupture of cysts in the liver happens frequently.

Some of the scolices which fall into the peritoneal cavity die, but those which become grafted undergo vesicular transformation. Through this change the scolices, instead of developing into taeniae (as they would have, had they been in a dog's intestine), turn into new hydatids equal to those formed at the expense of hexacanth embryos.

Secondary peritoneal hydatidosis can adopt two anatomic forms: the miliary hydatidosis of the peritoneum and the multiple hydatidosis. In the first instance, numberless scolices become attached to the serous membrane but do not undergo the vesicular transformation; they may resemble miliary tuberculosis. In the second form the scolices undergo the vesicular transformation and give rise to the formation of numerous cysts of variable size. These cysts are spread all over the peritoneal cavity, but especially in the declivitous regions and in the omentum majus.

This last form is often of a serious character, owing to the functional and mechanic disturbances caused by hundreds of cysts. Patients are subjected to countless series of operations to remove the larger ones or those which have undergone complications (septic cysts).

Another form of secondary hydatidosis is that which originates in the lung by the rupture of a cyst and the spread of its contents on the same

lung or the opposite one through the bronchial tree (bronchogenic hydatidosis).

BONE HYDATIDOSIS

The peculiarities offered by hydatidosis of the bones are such that I feel compelled to say a few words about them. As in other structures, the hexacanth embryo that reaches a bone through the blood stream and becomes attached to it undergoes vesicular transformation. However, little by little the hydatid vesicle is faced with true hostility on the part of the lodging structure, which has hard lamellas and lacks elements capable of reacting to the presence of the parasite. This resistance modifies the usual biologic tendency of the parasite. The vesicle finds its free growth hindered by the characteristics of the surrounding tissues. At the same time it is naked, without an adventitia; the walls of the cyst are in direct contact with the lamellae without any interposing connective tissue. The only elements that react in the presence of the cyst are those of the medulla ossium, and these surround the outer aspect of the chitinous membrane with a practically negligible adventitia.

From these facts are derived the characteristics of bone hydatidosis. Prevented from growing freely, the primary hydatid grows by producing exogenic daughter and granddaughter vesicles; these accumulate side by side until they form a conglomeration of hydatid vesicles capable of invading the entire bone, perforating the substantia compacta and the periosteum and even invading the soft parts. Therefore, bone hydatidosis is not unilocular but multilocular. The lack of an adventitia and the formation of exogenic vesicles which slowly infiltrate and destroy the osseous tissue without the latter attempting to defend itself show that there are no such things as hydatid cysts of bone (the blend of the parasite and the reaction of the host) but only an infiltrating hydatidosis, after the fashion of neoplasms.

Nevertheless, the biologic unity of the disease is still present. The proof of this assertion is the fact that if the bone becomes fractured and one or more hydatid vesicles fall among less hostile structures (muscle, subcutaneous tissue), their original tendencies reappear, and each gives rise to a unilocular hydatid cyst with an adventitia.

Bone hydatidosis is difficult to diagnose. Its evolution is slow and silent. Its presence is often suspected only as a result of the study of a roentgenogram taken after a pathologic fracture has occurred.

The prognosis is serious because of the difficulties of efficient treatment. The only treatment is the resection of the whole affected part, and the surgeon usually ignores the question as to how far this resection must be carried to make the treatment a success. Not long ago I resected one whole humerus of a woman, who fortunately is able to use her arm thanks to an excellent prosthetic apparatus which is now available.

CARCINOMA OF THE UPPER EXTREMITY

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Carcinoma of the upper extremity is not a common disease. Less than 10 per cent of all cutaneous lesions diagnosed as carcinoma occur at this site.[1] Heilman found 207 cases of carcinoma in which an upper or a lower extremity was the site among 2,054 cases of cancer; Broders, 44 cases in 2,000; DeAsis, 132 in 6,766.[2] In two thirds or more of the 207 cases the carcinoma occurred on an upper extremity. While prognosis is usually considered good, too frequently such a lesion is overlooked or undertreated.

TABLE 1.—*Conditions Present Preceding Carcinoma of Hand or Arm in Reported Cases*

	University of Michigan Series of Cases	Mason's Series of Cases	Mason's Collected Cases	DeBell's Series of Cases
Roentgen or radium irradiation	2	6	..	2
Trauma	2	7	20	25
Keratoses	10	..	..	
Verrucae	3	1	..	
Unchanged skin	..	2	..	
Condition unknown	..	3	..	
Scars other than from burns	..	..	21	
Scars from burns	2	..	19	5
Chronic inflammation	..	..	12	
Lupus vulgaris	1	..	10	1
Arsenical dermatitis	1(?)	..	2	

The etiologic factors were well outlined by Adair,[3] who expressed the belief that there are six main types resulting from: (1) changes of old age; (2) exposure to the elements; (3) previous burns; (4) internal medication; (5) prolonged chemical irritation; (6) roentgen or radium irradiation of the skin.

In the University of Michigan series in table 1 carcinomatous change occurring in keratoses was the largest proved etiologic factor.

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1. Mason, M. L.: Carcinoma of the Hand, Arch. Surg. **18**:2107-2158 (May) 1929.

2. Cited by DeBell, P. J., and Stevenson, T. D.: Squamous Cell Epithelioma of the Extremities, Surg., Gynec. & Obst. **63**:222-229, 1936.

3. Adair, F. E.: Epitheliomas of the Hand: Types and Treatment, S. Clin. North America **13**:423-433, 1933.

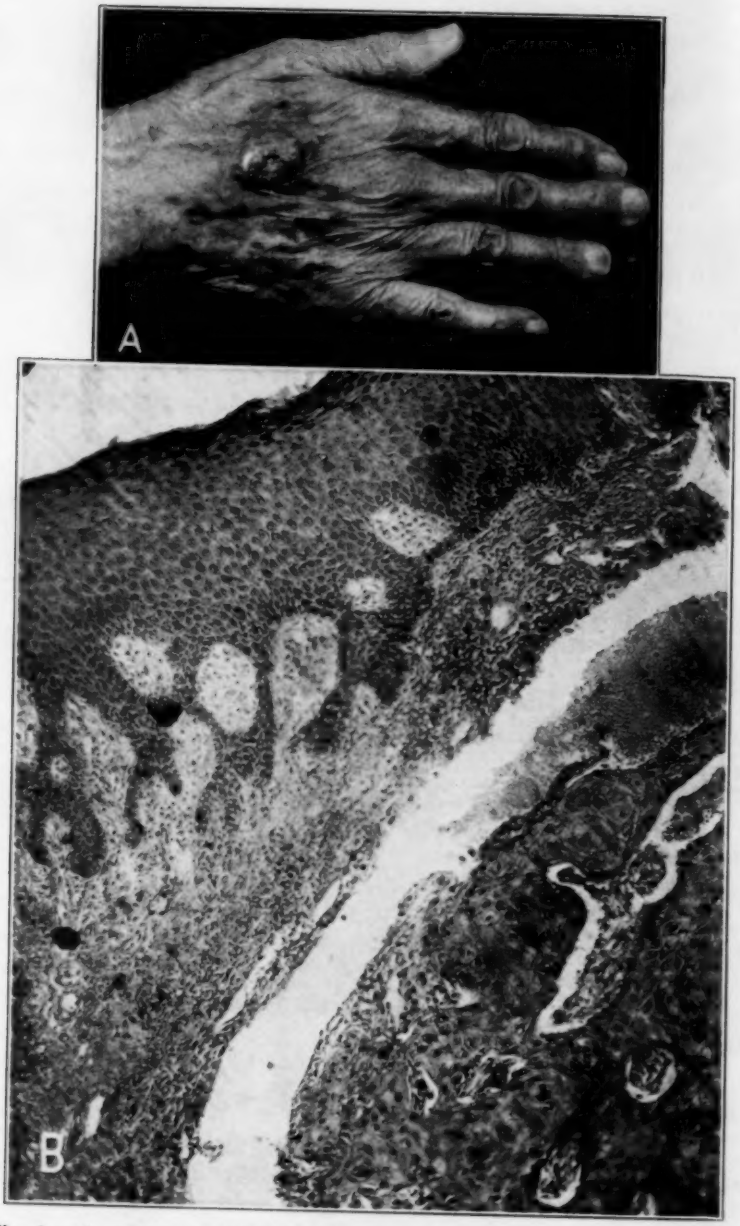

Fig. 1.—*A*, nodular nonulcerating lesion on the dorsum of the right hand of a 77 year old housewife after an abrasion previously at this site. She received roentgen therapy (1,000 r × 4). One year later the area previously treated by roentgen radiation was excised, but pathologic examination showed no evidence of malignancy. At the time of writing she is 81 years of age with no evidence of recurrence. *B*, photomicrograph of lesion before treatment.

Scars play a prominent part; in 19 of Mason's collected cases carcinoma developed in scars of old burns, and in 21, in scars from other injuries. Such trauma is probably a more important cause of carcinoma on the upper extremity than of carcinoma on other parts of the body, which are less subject to injuries.

Roentgen and radium irradiation have long played an important role in the production of carcinoma of the upper extremity, but from reports in the literature on this subject,[4] lesions caused by these procedures are becoming less frequent, a result probably of more careful technic in the use of roentgen and radium radiation and the less enthusiastic use of roentgen radiation in treating certain skin diseases. It has taken physicians approximately thirty years to heed the warning of Ouidin, who in 1897 first observed that dermatitis and epithelioma frequently followed roentgen irradiation of skin.[4b]

It has been estimated that lupus vulgaris accounts for cutaneous carcinoma in between 5 and 10 per cent of cases, and Mündelein [5] reported that in 3.2 per cent of all instances of lupus vulgaris this lesion undergoes malignant degeneration. The University of Michigan series contains 1 such case (fig. 2).

The patient first had a lesion of his left forearm at 6 years of age. Alternately healing and ulcerating, the lesion remained troublesome until the patient was 44 years old; at this time it remained healed for fourteen years. When 70 years old, he was admitted to the University Hospital because the lesion had been ulcerated for two years, and at this time carcinomatous degeneration was noted. Amputation was done through the upper arm, followed by prophylactic roentgen irradiation of the axilla. Microscopic examination of the epitrochlear nodes revealed no abnormalities. He died at 75 of a cerebral hemorrhage, with no evidence of recurrence.

An analysis of the 36 cases studied at the University Hospital reveals that 32 patients were men and 4 were women; a ratio of 8 to 1. Sixty-four per cent had lesions on the dorsum of the hand; 19.4 per cent, on fingers or thumbs; 8.3 per cent, on the wrist, and the same per cent, on the forearm. The average time since the patients were first seen at the hospital was twenty-nine and a half months. At the initial examination, 44.4 per cent of all the patients had palpable epitrochlear or axillary nodes or both, and 50 per cent of these suffered recurrence or ultimately died of the carcinoma.

In table 2 no figure is given for the University of Michigan series under "Per Cent Cured" because the criteria used by other authors in determining which patients should be listed as cured are not clear.

4. (*a*) Handley, W. S.: The Treatment of X-Ray Carcinoma on X-Ray Dermatitis, Lancet **1**:120-122, 1934. (*b*) Mason, M. L.: Carcinoma of the Hands and Feet, Surgery **5**:27-46, 1939.

5. Mündelein, W., quoted by Mason.[4b]

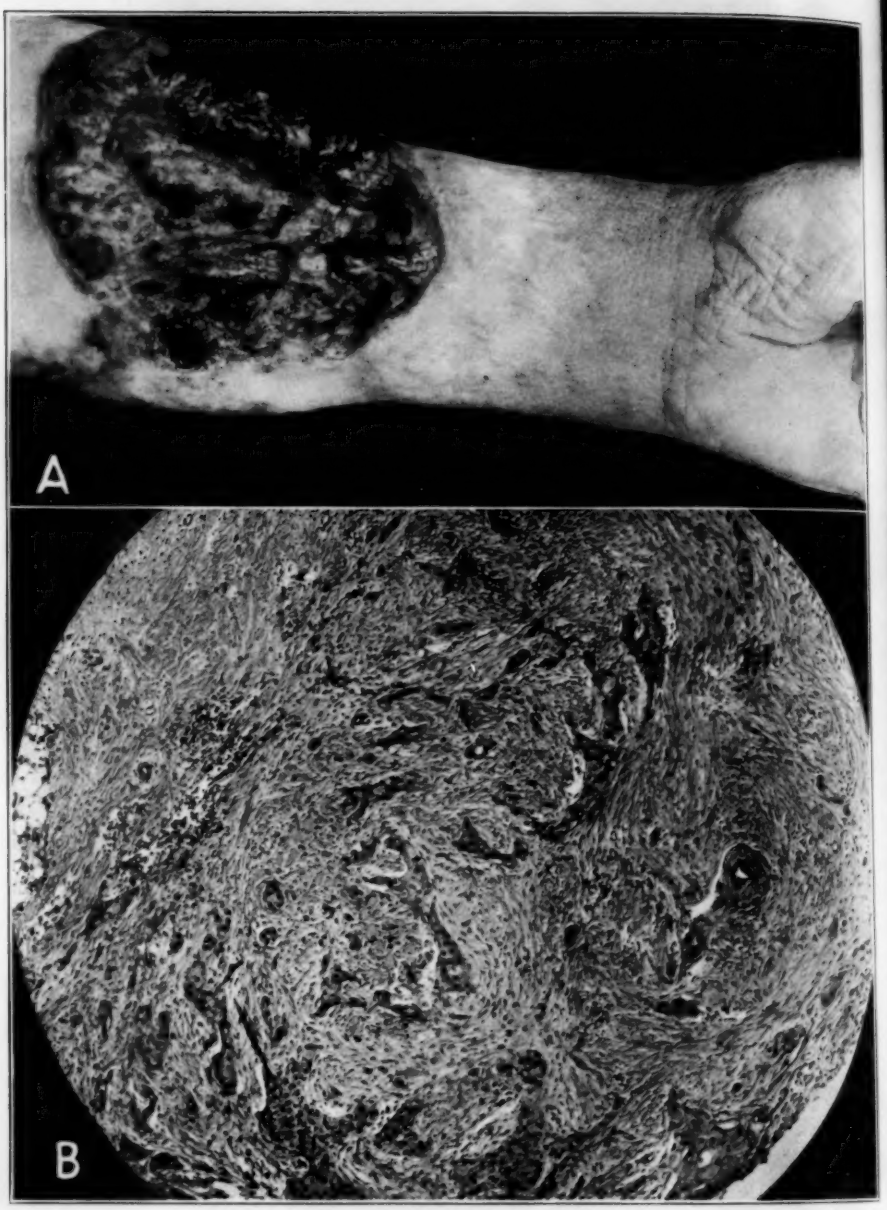

Fig. 2.—*A*, carcinomatous degeneration of lupus vulgaris mentioned in the text. The lesion was so far advanced that amputation through the upper part of the arm was done. The patient died five years later of a cerebral hemorrhage. *B*, photomicrograph of lesion.

TABLE 2.—*Comparison of Significant Features of Studies by Various Authors of Carcinoma of the Hand and Arm*

	Patients	Average Age	Ratio, Men to Women	Per Cent with Lesion on Dorsum	Per Cent with Metastases	Per Cent Cured	Ratio, Right to Left	Duration of Disease
Mason [1] (collected cases)...	232	59	2 to 1	....	....	..	2-1	"Long course"
von Brunn [6]	97	....	.....	....	....	35		
Mason [1]	25	59	2 to 1	94	51	65	1.6-1	2 to 3 years
Porter	...	....	.....	....	....	43.5		
Schreiner, B. F., and Wehr, W. H.: Am. J. Roentgenol. **32**: 516-523, 1934	101	....	.....	84	50	48		
DeBell, P. J., and Stevenson, T. D.: Surg., Gynec. & Obst. **63**: 222-229, 1936	51	58.3	3.5 to 1	70	37	72	...	1½ years
Broders [2]	...	....	4 to 1					
DeAsis [2]	...	...	2.5 to 1					
Univ. of Michigan Hosp....	36	61.6	8 to 1	63.8	44.4	..	1.1-1	29½ months

If five year periods of survivals are used to reach this figure, then only 11 per cent of the patients of this series have been cured, for only 4 patients have lived five years or more without recurrence. Many patients in the University of Michigan series, however, died of intercurrent disease, without evidence of recurrence, before the five year period was reached. If these can be included, 33 per cent of this series can be considered cured. Further, if all patients who have neither died nor suffered recurrence but who have not as yet reached the five year period of survival can be included, the per cent cured jumps to 72. This, ultimately, may become the true "per cent cured."

One interesting phase of this study is the incidence of coexistent malignant nepolasms in other parts of the body. Von Brunn[6] in 1903 noted 8 cases in which carcinoma of the extremity occurred separate from malignant neoplasm of some other structure. Other authors have either failed to record such an observation or considered it unimportant. In this series of 36 cases there were 18, or 50 per cent, in which other, proved unrelated neoplasms were present. All these were diagnosed as carcinoma of the skin (several were of the basal cell variety); 14 occurred on the face and 4 on other extremities.

In respect to the pathologic classification, 34 were squamous in type; 1 was mediocellular, and 1 was an adenocarcinoma of sweat gland origin.

The efficacy of treatment of these lesions has been subject to some debate, but operation and roentgen or radium irradiation of the site still remain the most popular procedures in the treatment of the local lesions as well as of the involved lymph nodes. Curet and cautery are occasionally employed for small local lesions. In the cases in which some type of surgical procedure was used for a local lesion, local excision, with and without graft, and amputation were the methods employed, as follows: local excision without graft, 3; local excision with graft, 10; amputation of finger, 4; amputation of arm, 2. Of these, recurrence has occurred in 1 case of local excision without the use of a graft.

Eleven patients were given active treatment to the lymph nodes. Six had roentgen radiation in fractionated doses; 1 of these ultimately died of his carcinoma. The remaining patients had no evidence of recurrence. Four had axillary and epitrochlear gland resection; 1 of these also died of his carcinoma. There was no evidence of recurrence in the remainder. One patient had both resection of axillary lymph nodes and roentgen radiation in fractionated doses to the axilla and ultimately succumbed to the effects of the carcinoma.

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6. von Brunn, M.: Ueber den primären Krebs der Extremitäten, Beitr. z. klin. Chir. **37**:227, 1903.

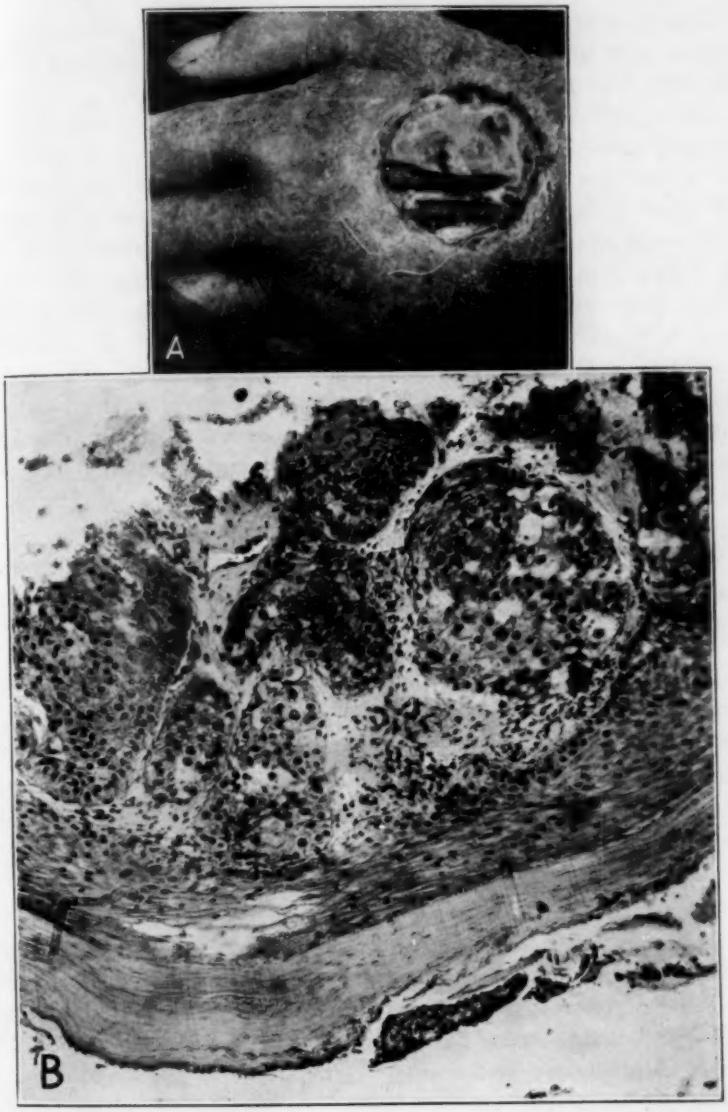

Fig. 3.—*A*, lesion on the dorsum of the left hand of an 81 year old farmer. The lesion when examined at the University Hospital was several years old. Four years prior to this examination he had received six roentgen treatments, which failed to cause regression in the size of the lesion. Excision by the local physician a year later appeared to be successful when the lesion remained healed for one year. Caustic irradiation (5,000 r × 2) at the University Hospital, and one month later local excision, left a defect which showed no evidence of healing. Accordingly, an amputation through the upper one third of the left forearm was done. The patient died of a coronary occlusion on the fourth postoperative day. *B*, photomicrograph of lesion.

Caustic or fractionated doses of roentgen radiation (and in 1 case radium) were used in treating the local lesion in 8 cases; in 4 of these there later was local recurrence.

Severe or widespread metastases were present at examination or developed subsequent to treatment in 9 patients, only 1 of whom was alive at the time of writing. This patient had surgical excision of the local lesion with fractionated doses of roentgen radiation to the axilla, and subsequently metastasis in an axillary node was discovered. The other 8 had metastases as follows: 2, axillary metastases; 1, cervical and pulmonary metastases; 1, axillary and pulmonary metastases; 2, widespread metastases revealed by necropsy; 1, widespread metastases, observed clinically; 1, a metastasis from another primary neoplasm. Of these patients, only 3 were actively treated: 1 had roentgen radiation to the axilla here after axillary dissection elsewhere; 1 had amputation of a finger with roentgen radiation to the axilla; 1 had amputation of an arm with axillary dissection and roentgen radiation to the axilla. The remaining patients had only biopsy for diagnostic purposes.

Although 15 patients of the 36 died, only 7 died of causes attributed directly to carcinoma. Eight died from intercurrent disease. It is interesting to observe that the average age of those dying from cancer was 52.7 years, whereas the average age of those dying from intercurrent disease was 75 years. Of the group dying from cancer, the 3 who had significant treatment lived thirty-four and six tenths months after treatment while those who had disease too far advanced to warrant active treatment lived twenty months after examination here. The average time of death after the institution of treatment in those patients dying from other causes was eighteen and six tenths months.

SUMMARY

Carcinoma of the hand or arm, although not frequent, is too often overlooked or undertreated. Vigorous early treatment must be carried out if good outcome is to be expected. In the experience of the University Hospital, wide surgical excision of the local lesion and a combination of surgical procedure and roentgen irradiation of the regional nodes have yielded the best results.

An analysis of 36 cases is presented.

INTESTINAL OBSTRUCTION

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I. POSSIBLE ROLE OF BACTERIA IN INTESTINAL OBSTRUCTION

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When one appreciates the breadth of physiologic applicability of the problem of intestinal obstruction, one can understand why the disorder has occasioned such an extravagant number of theories, prolific writings and extensive investigations. Unfortunately, too many glamorous sophisms have been dogmatically attached to attempted solutions of the problems presented by the group of disorders listed under the heading of intestinal obstruction.

Too often the physician conceives of the problem of obstruction as applying only to an acute mechanical blockage of the lumen of the intestine. It seems safe to assume that paralytic ileus from many causes not connected with direct mechanical obstruction of the lumen of the intestine may frequently, in the end, cause death by exactly the same processes as direct blockage of the lumen. Perhaps this applies in at least some instances to death from ileus secondary to peritonitis—death that would not occur were it not for ileus. It therefore does seem that when the unknown aspects of intestinal obstruction are solved, physicians will be able to apply this new knowledge more widely than to acute mechanical obstruction alone.

Though several excellent reviews on this subject have appeared within the past few years, it nevertheless seems desirable that we recapitulate the literature to a certain extent, in order to establish more clearly the premises on which we initiated the experimental work which we report in this paper.

This recapitulation and a discussion of the progress, or lack of it, which has been made toward establishing the true cause or causes of death in intestinal obstruction since the demonstration by Hartwell and

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Houget of the importance of the loss of fluids and essential salts may well be opened by quoting from the well known article of Murphy and Vincent [1]:

> There are three principal theories of the cause of death in acute intestinal obstruction, based on the observations of many clinicians and laboratory workers.
>
> 1. The theory of infection; that is, by the direct passage of organisms through the wall of the obstructed intestine into the peritoneal cavity, a fatal peritonitis is caused.
>
> 2. The theory of nervous reflex, which attributes the collapse and lethal result to the irritation of the nerve filaments of the intestinal wall.
>
> 3. The theory of auto-intoxication, which attributes the clinical symptoms to the absorption of some substance produced in the contents of the obstructed intestine. Attempts to determine the source of this toxic substance have divided the adherents of the theory of auto-intoxication into two groups. One group of investigators holds that the substance is due to the activity of the micro-organisms, which multiply within the obstructed intestine; the other believes that the essential factor is some disturbance in the secretion of the intestine itself.

For the sake of completeness the following theories may be mentioned in addition to those listed above:

> 4. Loss of blood and plasma into involved loops.
>
> 5. Destruction of tissue protein (loss of protein, excess of nonprotein nitrgoen and urea in the blood).
>
> 6. Hyperpotassemia.
>
> 7. Adrenal cortex insufficiency.
>
> 8. Failure of the contents of the upper part of the bowel to mix with the contents of the lower part.

The hyperpotassemia theory [2] (and the occurrence of hyperpotassemia as a morbid factor in the human being has been questioned) is not itself a complete hypothesis, since the hyperpotassemia when it occurs is secondary to alterations in the adrenal glands or other organs, the latter alterations being due to the primary toxic factors in obstruction.

There are many arguments against the theory that death occurs because the contents of the upper part of the intestine do not mix with the contents of the lower in obstruction. Whipple [3] made a specific experiment in this regard. He produced a closed loop in the duodenum just below the ampulla of Vater. He then established anastomosis between the stomach and the intestine below the obstruction permitting

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1. Murphy, F. T., and Vincent, B.: An Experimental Study of the Cause of Death in Acute Intestinal Obstruction, Boston M. & S. J. **18**:684, 1911.

2. Scudder, J.; Zwemer, R. L., and Whipple, A. O.: Acute Intestinal Obstruction, Ann. Surg. **107**:161 (Feb.) 1938.

3. Whipple, cited by Hewlett, A. W.: Pathologic Physiology, New York, D. Appleton and Company, 1916.

food, as well as bile, pancreatic juice and gastric secretion, to pass freely into the unobstructed part of the intestine. The dogs thus treated died in from thirty-six to seventy-two hours.

In speaking of adrenal cortex insufficiency Wohl and co-workers [4] said: "Indeed, we described the histologic changes of the adrenal gland in the dog with high intestinal obstruction as that of lipoid exhaustion of extreme degeneration of the adrenal cortex." They stated that Kendal had separated two fractions from extract of adrenal cortex, one which produced results when salt was administered with it. They emphasized the many features in common between acute intestinal obstruction and adrenal cortex insufficiency and also emphasized the apparent benefit from combined administration of physiologic solution of sodium chloride and adrenal cortex extract in combating the toxemia from high intestinal obstruction. Certainly, however, degeneration of the adrenal cortex when it occurs, like hepatic degeneration,[5] is an end result of more fundamental and primary alterations, which undoubtedly can cause death in the absence of either hepatic or adrenal cortex degeneration.

It is now generally accepted that the patient with high obstruction may die from a loss of fluid and salts if substitution therapy is not instituted even though strangulation or marked distention does not occur. Exclusive of this cause of death (loss of fluids and salts), the nerve reflex theory (next to the autointoxication theory) is probably the most popular at present.

A discussion of the nerve reflex theory was recently presented by Antoncic and Lawson.[6] They cited the work of Herrin and Meek,[7] who placed in the intestines of dogs balloons having pressures of 50 to 80 mm. of mercury. Herrin and Meek disposed of the toxin as the cause of death when they found that despite free drainage of Thiry-Vella nondenervated loops death occurred in the animals, whereas when they denervated draining loops they prolonged the lives of some of their animals.

Antoncic and Lawson in support of their arguments also mentioned that Ender and Herrin [8] divided the jejunum 25 cm. from the ligament

4. Wohl, M. G.; Burns, J. C., and Pfeiffer, G.: High Intestinal Obstruction in the Dog Treated with Adrenal Cortex, Proc. Soc. Exper. Biol. & Med. **36**:549 (May) 1937.

5. Boyce, F. F., and McFetridge, E. M.: Acute Intestinal Obstruction, South. Surgeon **6**:109 (April) 1937.

6. Antoncic, R. F., and Lawson, H.: The Neurogenic Factor in Intestinal Obstruction, Surg., Gynec. & Obst. **72**:728 (April) 1941.

7. Herrin, R. C., and Meek, W. J.: Distention as a Factor in Acute Intestinal Obstruction, Arch. Int. Med. **51**:152 (Jan.) 1933.

8. Ender, E. C., and Herrin, R. C.: The Relative Importance of Toxemia in Jejunal Obstruction in Dogs, Am. J. Physiol. **126**:P485 (July) 1939.

of Treitz, inverted both ends of the sectioned bowel by means of a purse string suture and anastomosed the caudad end to the stomach or to the lower portion of the duodenum. The fluid from the obstructed bowel was returned to the normal bowel so that there was only slight loss from vomiting. Four dogs thus treated lived eight days, two weeks, four weeks and six weeks, respectively. The death on the eighth day was preceded by perforation of the bowel. These investigators (Ender and Herrin) then denervated the loops of 2 animals which had been operated on as described. One of these animals remained without symptoms for sixteen days and then died within a few hours after the onset of symptoms. The other dog with a denervated loop was reported normal on the eighteenth day of obstruction. Since the dogs survived "far beyond the eight days," excepting the one with perforation, they concluded that toxemia is of less importance in acute obstruction than chemical or nervous factors.

Taylor and associates [9] prolonged for hours the lives of dogs whose intestines were distended with balloons by placing next to the balloons, in the intestinal lumens, a by-pass of heavy-walled rubber tubing and concluded that efferent nerve impulses are an important factor in death.

Other investigators—for instance, Fine and co-workers [10]—concluded that resection of splanchnic nerves and exclusion of the afferent nerve supply from obstructed loops do not influence the survival time of animals with intestinal obstruction.

Antoncic and Lawson [6] themselves produced obstruction of the jejunum 15 cm. from the ligament of Treitz by resecting a 10 to 12 cm. segment and inverting the ends to form a closed loop. They reestablished the continuity of the gastrointestinal tract by an end to end anastomosis. Of 10 nondenervated control animals thus treated, all died in thirty-six hours to seven days, the average period being approximately seventy-two hours. At autopsy 7 dogs had perforation, and 3 dogs distention, of the loops. Of 23 dogs in which the nerve supply of the isolated loop had been destroyed, 12 died in three to four days, and 11 lived longer. At autopsy of the 12 animals which died, the loop of 1 dog was found perforated, and death was attributed by Antoncic and Lawson to peritonitis. Five of the 11 which lived longer than three to four days were killed in from four to eight weeks and while they were considered normal. These animals did not vomit after the first day or two, ate well and were active and alert. Postmortem examination showed that 3 of the 5 killed dogs had collapsed loops containing 10 to 20 cm. of gray mucous fluid, while

9. Taylor, N. B.; Weld, C. B., and Harrison, K.: Experimental Intestinal Obstruction, Canad. M. A. J. **29**:227 (Sept.) 1933.

10. Fine, J.; Rosenfeld, L., and Gendel, S.: The Role of the Nervous System in Acute Intestinal Obstruction, Ann. Surg. **110**:111 (Sept.) 1939.

2 had "markedly distended" loops. A culture from one of the latter yielded a pure growth of hemolytic and nonhemolytic streptococci. The remaining 6 animals of the group of 11 died in from three to four months and were considered entirely normal until one to three days before death, when they became listless, vomited and refused to eat. The authors made the following comment:

> Four dogs dead of internal herniation and volvulus apparently had acute accidents avoidable with better surgical technique. Why two animals should suddenly develop a generalized acute gangrene after 3 and 4 months of normal livelihood is not apparent.

In the face of the work just reviewed and the comments relative to the part of nerve reflexes in the morbid picture it is interesting to quote again from the article of Murphy and Vincent of 1913:

> While the nerve reflex theory might explain the symptom-complex, no positive evidence supporting this theory has been produced. Moreover, section of the splanchnics which wholly disconnects the intestine from the central nervous system fails to alter in the least the fatal course of the infection. Therefore, in our opinion, the nerve reflex theory, which may account for some of the early symptoms, fails to furnish a basis for a satisfactory explanation of the fatal course.

We believe that the foregoing statement of Murphy and Vincent still holds today. Certainly, though the work of Antoncic and Lawson is a worth while contribution to the literature, it and the previous work cited by these men as contributing to proof of the neurogenic factor in death cannot be taken as conclusive. Of the 5 dogs in the series of Antoncic and Lawson killed in four to eight weeks, animals which were considered normal at the time they were killed, 3 were found to have collapsed loops. In 2 of the animals the isolated loops were considered "markedly distended," but "markedly distended" is an insufficient description on which to base the conclusion that the dogs' lives had been prolonged by denervation of the loops. And as to the 6 animals with denervated loops which lived for three weeks to four months, surely the degree of distention of the loops during the interim was unknown. Undoubtedly, severe and consistent distention was not present or perforation of the loops would have ensued from interference with the blood supply. And it is unusual that 4 of the 6 dogs died of "internal herniation and volvulus," an "acute accident avoidable with better surgical technique." The remaining 2 of these 6 dogs died of gas bacillus infection.

Albeck [11] was one of the few investigators who worked with strangulated loops previous to 1913. He strangulated loops of ileum from 15 to 20 cm. long and advocated the autointoxication theory

11. Albeck, V.: Arch. f. klin. Chir. **65**:569, 1902.

previous to Murphy and Vincent. Albeck, as quoted by Murphy and Vincent, concluded that:

1. The material obtained from these obstructed [strangulated] loops, when injected into other animals, reproduces these typical symptoms [of obstruction].

2. This material, after being passed through a Chamberland filter, is still toxic for the injected animal.

3. The extract of the intestinal content, even after boiling, is toxic.

Albeck believed the toxic substance was due to the putrefactive poisons.

As cited by Murphy and Vincent, the observations of McClure[12] are interesting because he showed that when bile and pancreatic juices were diverted from the obstructed intestine toxemia developed nevertheless; in other words, the toxin of obstruction, according to McClure, was formed independently of the pancreatic and biliary secretions.

Murphy and Vincent concluded that Kukula, Albeck, Borszeky and Genersich, Clairmont and Ranzi, McClure, Braun and Boruttau had published the most exhaustive and suggestive articles in support of the bacterial origin of toxic agents in intestinal obstruction up to the time of their report in 1913. But they emphasized that practically all previous workers with the exception of Albeck had worked with obstructions other than strangulation. Murphy and Vincent considered the various methods of approach to the solution of the autointoxication problem and the lack of agreement of workers as inconclusive. They therefore themselves ligated in cats either the venous or the arterial blood supply or both to closed unwashed loops of small bowel at various levels (in each instance sufficiently extensively to produce gangrene in the closed loop). They then demonstrated that material from the *unobstructed* small bowel was relatively nontoxic when injected intraperitoneally into other animals. All the animals with ligation of the blood supply to an obstructed bowel died within approximately twelve to twenty-four hours, and the material from the loops when injected intraperitoneally into other animals proved to be very toxic.

They then studied the effect of heat and filtration on the material obtained from the involved loops.

They concluded that strangulation of the blood supply to an involved loop was the vital factor in the production of toxin in obstruction and that the toxin was produced within four to six hours after interference with the blood supply. They demonstrated that the toxic substances produced were destroyed by boiling, were not soluble in water and would not pass through a Berkefeld filter.

12. McClure, R. D.: An Experimental Study of Intestinal Obstruction, J. A. M. A. **49**:1003 (Sept. 21) 1907.

Knight and Slome [13] recently contributed an instructive study, which has been rather widely cited and commented on editorially. They worked with the closed loop of small intestine, the latter being strangulated at about the midportion. The loop was unwashed in every case except the one to be mentioned. They demonstrated a marked depressor toxin in the loop of strangulated intestine, which appeared within thirty minutes after strangulation, and concluded that because of the rapidity of appearance the toxin could not be bacterial in origin. They admitted, however, that bacterial invasion of devitalized tissue and subsequent proteolytic action might later produce further toxic substances from the tissues of the intestinal wall other than their depressor substance. They stated that they were not yet in position to identify the substance or substances concerned with the depressor reaction but cited the work of Euler and Gaddam [14] as demonstrating that muscle of intestine is the source of a depressor substance which evokes a blood pressure reaction very similar to those which have already been described. They also mentioned the work of Lim, Ling and Liu,[15] who prepared an extract from intestinal mucosa and demonstrated effects which were even more comparable to those of their depressor substance. Lim and co-workers expressed the belief that this extract was a small mixture of histamine with the Euler-Gaddam-Fliex-Lange substance and that its effect was not due to acetylcholine, adenyl compounds, kallikrein or Major's non-guanidine depressor substance.

Knight and Slome stated that their depressor substance was different from the toxic proteose described by Whipple and co-workers,[16] since it was dialyzable. Whipple and co-workers had concluded that impaired mucous membrane produced the lethal factor and that nothing produced in the lumen of the intestinal tract was concerned in the cause of death.

Knight and Slome, in order to determine whether the depressor substance was produced in the tissues of the intestinal wall or was a substance already present in the intestinal lumen which was absorbed following strangulation, divided the intestine transversely distal to the pylorus as well as above the ileocecal ends which had been severed and inserted a cannula into each end of the isolated segment of intestine.

13. Knight, G. C., and Slome, D.: Intestinal Strangulation, Brit. J. Surg. **23**:820 (April) 1936.

14. Euler, U. S., and Gaddam, J. H.: An Unidentified Depressor Substance in Certain Tissue Extracts, J. Physiol. **72**:74 (June) 1931.

15. Lim, R. K. S.; Ling, S. M., and Liu, A. C.: Depressor Substances in Extracts of Intestinal Mucosa, Chinese J. Physiol. **8**:219 (Aug. 15) 1934.

16. Whipple, G. H.; Rodenbaugh, F. H., and Kilgore, A. A.: Intestinal Obstruction Versus Proteose Intoxication, J. Exper. Med. **23**:123 (Jan.) 1916. Whipple, G. H.; Stone, H. B., and Bernheim, B. M.: Intestinal Obstruction, ibid. **17**:286 (March) 1913.

They then washed out the intestinal lumen with 4 to 5 liters of warm water until the washings were clear. The water was then displaced with air and about 80 to 100 cc. of warm saline solution introduced. After half an hour the saline solution was displaced and an equal volume of fresh saline solution introduced. The intestine was then strangulated by ligating the superior mesenteric vein for a period of one hour. At the end of this time the saline solution was again displaced from the lumen and a sample of blood removed from a mesenteric vein. Two samples of saline solution from the lumen were thus obtained, the first from nonstrangulated intestine and the second from strangulated intestine. Each sample was filtered and the filtrate centrifuged. The first sample appeared clean and the second slightly blood stained. These samples were then tested by being injected intravenously into the normal animals, and in every case it was found that whereas saline solution from the nonstrangulated intestine was without effect, the washing from the intestinal lumen after the intestine had been strangulated for one hour was definitely depressor.

It has been known for many years that in many cases of obstruction (not all) there is considerable destruction of tissue protein with excessive amounts of nonprotein nitrogen and urea in the blood. Well informed clinicians as well as experimental investigators now recognize that in any disorder accompanied by loss of protein or low intake of protein replacement of the lost protein or supplementation of the ingested protein (by blood plasma, blood or prepared protein) is often as essential as the administration of the more commonly used fluids (dextrose and saline solutions). Several investigators have called attention to the deleterious loss of blood and plasma into obstructed loops and have expressed the belief that shock from such loss may cause death. Knight and Slome, however, reported a series of experiments from which they concluded that loss of fluid "plays at most only an accessory role in the production of circulatory collapse resulting from medium loop strangulation." After study of long loop strangulations they disagreed with Holt [17] and stated that they did not consider even the hemorrage or loss of fluid into these long loops as being responsible for death in intestinal obstruction and that certainly if death did result from such a cause it did so exceptionally. Our own opinion, based on the literature as well as on experimental work on venous mesenteric occlusions, leads us to agree with this statement of Knight and Slome. And though protein therapy in the form of administration of blood plasma is of great benefit when sudden or slow loss of plasma or of tissue protein has occurred, we know of no work which has proved it to be life saving in itself when absorption

17. Holt, R. L.: The Pathology of Acute Strangulation of the Intestine, Brit. J. Surg. **21**:582 (Oct.) 1934.

of products associated with markedly degenerating intestinal tissue is permitted to continue.

Kocher,[18] as early as 1877, working with strangulated intestines in rabbits, concluded that peritonitis was not the cause of death in intestinal obstruction, and a sufficient number of subsequent workers have confirmed his opinion.

Nesbitt,[18] studying the intestinal contents above occlusion of the small intestine in dogs which were fed food rich in lecithin, obtained choline and neurine and expressed the belief that these were lethal factors.

. Gerard [19] reported that he had demonstrated histamine as a toxin of intestinal obstruction.

Murphy and Brooks [20] isolated a closed intestinal loop and reestablished the continuity of the bowel. They found that when the closed intestinal loop was rendered sterile by long-continued drainage and then was closed it was compatible with life even though strangulated. Dragstedt and associates [21] found that the closed intestinal loop was compatible with life if the bacteria in the loop had been eliminated by drainage before closure.

Haerem, Dack and Wilson [22] and others have concluded from experiments that Williams [23] was incorrect in assuming that Welch bacilli have something to do with toxicity in intestinal obstruction. Williams advanced this hypothesis in 1926. He passed the intestinal fluid from the obstructed loops through a Berkefeld filter. He injected 0.75 cc. of the filtrate with 0.25 cc. of normal horse serum into mice intramuscularly; into another group he injected 0.75 cc. of filtrate together with 0.25 cc. of Welch antitoxin. He tabulated striking results showing large numbers of deaths in the first group and none in the second. The mice were observed for six days.

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18. Cited by Ellis, J. W.: The Cause of Death in High Intestinal Obstruction, Ann. Surg. **75**:429 (April) 1922.

19. Gerard, R. W.: Chemical Studies on Intestinal Obstruction, J. Biol. Chem. **52**:111 (May) 1922.

20. Murphy, F. T., and Brooks, B.: Intestinal Obstruction: An Experimental Study of the Causes of Symptoms and Death, Arch. Int. Med. **15**:392 (March) 1915.

21. Dragstedt, L. R.; Moorhead, J. J., and Burcky, F. W.: Intestinal Obstruction in Closed Intestinal Loops, J. Exper. Med. **25**:421 (March) 1917. Dragstedt, L. R.; Dragstedt, C. A.; McClintock, J. T., and Chase, C. S.: Intestinal Obstruction, ibid. **30**:105 (Aug.) 1919.

22. Haérem, S.; Dack, G. M., and Wilson, H.: Acute Intestinal Obstruction: Role of Bacteria in Closed Jejunal Loops, Surgery **3**:333 (March) 1938.

23. Williams, B. W.: Importance of Toxemia Due to Anaerobic Organisms in Intestinal Obstruction and Peritonitis, Brit. J. Surg. **14**:295 (Oct.) 1926.

Haerem, Dack and Wilson used a closed loop of the upper part of the jejunum; the length in the different animals varied from 15 to 30 cm. They sectioned the loop at each end and closed the ends by purse string sutures; then they reestablished the continuity of the bowel around the loop.

> When the animals appeared to be critically ill, usually thirty-six to seventy-two hours after operation, a second laparotomy was done and the obstructed loop removed. The fluid from this excised loop was immediately placed in sterile containers and used for bacteriologic examination and toxicity studies.
>
> The loop contents were centrifugalized at high speed for forty-five minutes and the supernatant fluid carefully removed and used for mouse inoculations. Mice weighing from 17 to 20 Gm. were given from 0.2 cc. to 0.5 cc. of fluid intravenously, control animals being given the same quantity together with 0.05 cc. of Cl. *welchii* antitoxin. Deaths of mice occurring within forty-eight hours only were recorded.

A strain of Welch bacilli, which in most instances was capable of producing a potent toxin in vitro, was isolated for each animal. The investigators did not heat or filter the loop fluid before it was injected, feeling that prolonged filtration or heating might destroy the Welch toxin. They concluded that the Welch toxin was not the specific toxin of death in acute intestinal obstruction.

Trusler and Reeves [24] and others have called attention to the great variability in toxicity of Clostridium welchii. They quoted Brown and agreed with him, stating:

> Brown, in a comprehensive study of anaerobic bacteria, has shown the variability of sugar fermentation even within a single strain. He concludes that anaerobes are divided into groups according to their ability to ferment sugars, and according to their proteolytic powers, but that they cannot be rigidly divided as being either saccharolytic or proteolytic. We have found that C. Welchii regularly ferments dextrose, sucrose, maltose and lactose with acid and gas, and that its proteolytic powers are very limited.

The organisms occupying the livers and muscles of the dogs studied by Trusler, Reeves and Martin did not produce an exotoxin but were all large gram-positive bacilli. Their morphologic characteristics and gas production could easily have permitted confusion of them with pathogenic forms when actually they were not pathogenic.

EVALUATION OF THE PRESENT STATUS OF THE LITERATURE AS TO FUNDAMENTAL LETHAL FACTORS

The greatest mass of evidence available at present indicates that there are two fundamental "chief concerns" in any given case of acute intestinal obstruction: first, loss of fluids and electrolytes; second,

24. Trusler, H. M., and Reeves, J. R.: Significance of Anaerobic Organisms in Peritonitis Due to Liver Autolysis, Arch. Surg. **28**:479 (March) 1934.

interference with the blood supply. And since, as far as we know, the problem of replacement therapy (fluids and electrolytes, proteins in the form of blood plasma, blood and prepared proteins) has been rather well solved with regard to acute obstructions, the most serious primary concern in any case is usually the interference with the blood supply. This interference may come by direct obstruction of the mesenteric vessels to an intestinal segment as in strangulating volvulus or in mesenteric thrombosis; or, according to Gatch, Wangensteen, Van Buren, Sperling and others who have done careful experimental work in this regard, it may be produced by bowel *distention*. Gatch and Culbertson [25] concluded from their study that "intraintestinal pressure as low as 20 mm. of mercury produces an almost complete anemia of the mucosa of the bowels"; again Gatch, Trusler and Lyons [26] concluded from an experimental study that relatively low intraintestinal pressure, namely, 20 to 40 cm. of water, allows for damage and the onset of lethal factors in an obstructed bowel.

Wangensteen has made a great contribution toward control of interference with blood supply from distention in simple obstructions. And the Miller-Abbott tube combined with suction may be used still more effectively to decompress greater lengths of intestine in some instances. But, as Wangensteen himself warned, decompression therapy has not solved the entire problem of the interference with blood supply. Obviously, a closed loop obstruction cannot consistently be decompressed by Wangensteen suction or the Miller-Abbott tube, and when gangrene of the intestine is present the decompression therapy can be used only as an adjunctive treatment, the most imperative problem being to rid the body of the gangrenous intestinal tissue.

It is true that no one has proved that neurogenic factors associated with distention, adrenal cortex alteration, splanchnic dilatation, loss of fluid into the involved loop, disturbances of blood plasma volume, destruction of tissue protein and hyperpotassemia are not from time to time all complicating elements in the morbid picture. It is possible that some of these factors at times may assume an important role in the immediate final cause of death. But, as said, it seems that stress has been laid too frequently on these "secondary factors" to the neglect, especially, of the fulminating factors which arise from serious interference with blood supply.

Of course, if some specific end result of interference with blood supply, such as hyperpotassemia or adrenal cortex insufficiency, could

25. Gatch, W. D., and Culbertson, C. G.: Circulatory Disturbances Caused by Intestinal Obstruction, Ann. Surg. **102**:619 (Oct.) 1935.

26. Gatch, W. D.; Trusler, H. M., and Lyons, R. E.: Toxemia in Acute Intestinal Obstruction, Arch. Surg. **28**:1102 (June) 1934.

be demonstrated as the specific cause of death secondary to the interference with blood supply, and some specific therapy could be rendered to counteract this immediate cause of death, then indeed would a step forward have been made. But no specific medical therapy has as yet been demonstrated as effectively slowing the tremendously rapid physiologic collapse which follows immediately on devitalization of intestinal tissue. But one must accept that as long as investigators are unable to prove more emphatically the exact nature of the toxins produced—for various investigators have repeatedly produced toxins from the intestinal wall uncontaminated by substances normally found within the intestinal lumen—that until the chemical nature and the pharmacologic effects of these toxins in other animals are well known, there will continue to be considerable confusion and discussion of many theories. And such confusion will, of course, cause uncertainty in the minds of physicians relative to the treatment of obstruction.

In evaluating the present status of the research and the clinical aspects of the problem it may be said that the past three decades have been a period in which investigators have traveled in a widening circle. They have stored additional and valuable knowledge in their files, and much of it may later prove to be of more practical value than it is at present. But if they are to clarify fully the problem of obstruction they must answer still more accurately and repeatedly the old fundamental questions:

1. Is there a lethal toxin or toxins liberated by degenerating intestinal wall which will produce death despite all present methods of therapy unless absorption of such products is stopped early?

2. If such toxin or toxins are present, what role do bacteria play in their production? Are toxins of bacteria themselves the lethal factor? Or are the toxins formed by the bacteria acting on the devitalized intestinal tissue?

3. Are toxic products which are normally present within the intestine absorbed as the injured wall becomes more permeable and are they a lethal factor?

4. If toxic products of protein degeneration are present, what is their nature? Are they absorbed in sufficient quantity to cause death and what is the pharmacologic action of such toxins?

METHODS AND OBJECTIVES OF OUR EXPERIMENTAL PROCEDURES

We set about with the purpose of, so far as possible:

1. Obtaining as pure and uncontaminated products of degeneration as we could from the *wall* of the small intestine at an early hour after ligation of the blood supply to the loop selected.

2. Selecting sufficiently small animals for injection of the products of degeneration to permit us to have a larger series of experimental animals on which to study the pharmacologic effect of toxin than would be possible in proportion if the products were injected in larger quantities into fewer animals.

3. Establishing control studies to demonstrate the relative nontoxicity of secretions from the clean wall of the nonstrangulated intestine.

4. Determining whether bacteria are essential to the production of any toxin found.

5. Determining whether the toxin of the bacteria themselves could be a factor.

6. Studying the chemical nature of any toxin produced.

We do not claim to have decisively attained all the stated objectives, but the experiments have been done carefully, and we have every confidence that if other investigators proceed with the same meticulous effort along exactly the same lines of procedure, they will be able to confirm our conclusions so far as they go.

GROUP I

STUDY OF NONSTERILE NORMAL SECRETIONS

The objective in this group was to ascertain whether the normal ileac secretions of dogs were toxic to mice when injected intraperitoneally in quantities equal to lethal doses (by volume) of the secretions obtained after ligation of the blood supply.

Ten dogs were used in this group.

Some preliminary experiments not listed here were done as we established the standard dose of 8 minims (0.5 cc.) for the intraperitoneal injections, which was the dose generally used in this and subsequent groups.

Dog 7, series 8A, was operated on under ether anesthesia, with no preliminary medication, Feb. 9, 1939. At 11:20 a. m., a 15 inch (38 cm.) loop of the lower part of the ileum was isolated and thoroughly washed with tap water running through a tube until all gross matter had been removed and the return was perfectly clear. The loop was then stripped "dry." The blood vessles and lymphatics to the loop were *not* tied. All ends of loop and intestine were closed without any medicaments being instilled into the loop. The latter was then returned to the abdomen. At 1:24 p. m. of the same day (giving a two hour specimen) the abdomen was again opened, without anesthesia, and about 45 cc. of moderately clear thin fluid was obtained from the loop. The latter was then closed and returned to the abdomen.

Promptly 8 minims of this unfiltered, untreated, undiluted fluid was injected intraperitoneally into each of 4 mice. All the mice recovered and did not seem ill at any time.

The abdomen of the dog was opened again at 4:15 p. m., and 30 cc. of the same kind of fluid was taken from the then distended loop, and 8 minims injected intra-

peritoneally into each of 3 mice. These mice recovered. All the injections of both specimens were made promptly after the removal of the fluid from the loop.

Gram-stained smears, 1 cm. square, of the loop fluid were examined with results as follows: Specimen of 11:13 p. m. (from washed intestinal wall), 0 bacteria per oil immersion field; specimen of 1:45 p. m., 0 bacteria per oil immersion field; specimen of 4:15 p. m., 1.5 gram-positive rods (morphologically Cl. welchii) to the oil immersion field.

Four additional dogs were treated in exactly the same manner as described for dog 7, series 8A; smears of the relatively clear fluid obtained were examined, and each specimen from each dog was injected intraperitoneally into 5 mice. The specimens presented bacterial counts running from 0 to 10 micro-organisms per oil immersion field (the micro-organisms being morphologically almost exclusively Cl. welchii). All of the 20 mice recovered except 4 (2 received specimens from each of 2 dogs, the specimens containing 8 to 10 micro-organisms per field). These 4 mice died in thirty-six to forty-eight hours.

In 2 additional dogs there was insufficient fluid in the loops at two and four hours to permit intraperitoneal injections in mice.

In 3 other dogs the loop fluid in five hours showed 30 to 200 micro-organisms resembling Cl. welchii per oil immersion field. Material from the loops of the 3 dogs was injected into 25 mice and all except 1 mouse died within twenty-four hours. Autopsy of the mice left us undecided as to whether the animals died of peritonitis.

CONCLUSIONS FROM GROUP I

1. Thin, relatively clear, untreated, nonsterile, fresh, normal ileac secretions from dogs are not lethally toxic to mice when injected in relatively large doses (8 minims) intraperitoneally provided the bacterial content of the fluid is low (arbitrarily below 8 to 10 micro-organisms per oil immersion field).

2. Normal fresh ileac secretions mixed with flocculent products (probably protein in nature) from the ileum and showing a high bacterial count (micro-organisms having the morphologic characteristics of Cl. welchii) kill mice within twenty-four hours when injected intraperitoneally in 8 minim doses.

GROUP II

A CONTROL DETERMINATION OF THE TOXICITY OF NONSTERILE SECRETIONS FROM ILEAC LOOPS WITH STRANGULATED BLOOD SUPPLY

Having determined by the experiments of group I that the normal nonsterile secretions were not lethal or apparently toxic to mice on intraperitoneal injection in 8 minim doses if the bacterial counts on smears from the secretions were low (arbitrarily 8 to 10 micro-organisms per oil immersion field or less), we next injected into mice 8 minim doses of nonsterile secretions from lower ileac loops to which all of the blood supply had been ligated.

Eight dogs were used in this group. The technic of the production and collection of fluid, as illustrated in the following protocol, was the same for each experiment.

Dog 8, series 8A, was operated on March 18, 1939 at 9:05 a. m., under ether anesthesia, with no preliminary medication. About 15 inches of the lower part of the ileum was isolated, the open ends of the bowel from which the loop had been detached were promptly closed, all arteries and vessels to the loop were ligated, and the loop was washed thoroughly by running tap water until the return was completely clear; the loop was then stripped dry and returned to the abdomen. At 12:30 p. m. (giving a three hour forty-five minute specimen) 22 cc. of bloody fluid was collected; the loop was closed and returned to the abdomen.

Gram-stained smears, 1 cm. square, of this specimen showed 12 bacilli (morphologically Cl. welchii) per oil field. No other bacteria were seen.

Intraperitoneal injections were made in thirty-one mice. The results may be summarized without taking space to report the experiments in greater detail. We had previously demonstrated that the intraperitoneal injection of 1 cc. of fresh polyvalent Bacillus perfringens antitoxin (Lilly) does not kill full grown mice.

SUMMARY OF STUDIES OF GROUP II

Eight minim doses of the nonsterile fluid obtained from cleansed loops of ileum three hours and forty-five minutes after the ligation of the blood supply to the loops and injected intraperitoneally into mice killed all the mice.

The only micro-organisms found on Gram-stained smears were gram-positive and were morphologically Cl. welchii. The only additional identification procedure used was the usual milk culture, which also indicated Cl. welchii.

Intraperitoneal and subcutaneous injections of fresh polyvalent B. perfringens antitoxin in 1 cc. doses did not protect mice from these nonsterile products procured from ileac loops after the blood supply to the loops had been ligated for three hours and forty-five mintues. No demonstrable protection was obtained when the fresh toxic loop fluid was mixed with an equal amount of the fresh polyvalent antitoxin and the mixture allowed to stand in a test tube for a period of forty-four minutes before being injected intraperitoneally.

It could be legitimately argued that peritonitis alone killed these mice. The manufacturers of the B. perfringens antitoxin do not claim that the product destroys bacteria. However, autopsies of the mice left us uncertain that any of the animals died of peritonitis. Furthermore, the majority of the mice survived intraperitoneal injections of 8 minim doses of nonstrangulated loop fluid containing only 12 of the micro-organisms with which we were working, per oil immersion smear. Therefore, though the studies of this group are not conclusive in themselves, we report them even though they were preliminary to the investigations, the reports of which follow.

GROUP III

THE TOXICITY OF FRESH MATERIAL FROM ILEAC LOOPS THE BLOOD SUPPLY OF WHICH HAD BEEN STRANGULATED (MATERIAL MADE STERILE BY BERKEFELD FILTRATION PREVIOUS TO INJECTION INTO MICE)

Having by the previous two groups of experiments partly reached a control basis from which to carry on the future experiments herein listed, having established that the normal secretion from ileac loops is in itself not lethal to mice in intraperitoneal 8 minim doses and having established that intraperitoneal 8 minim doses of nonsterile ileac secretion collected from the loops between three and four hours after the blood supply to the loops had been ligated were lethal, we set about to determine as best we could whether bacteria were necessary for the production of toxins in a strangulated loop and to determine whether bacteria were necessarily a cause of death by peritonitis in mice given intraperitoneal injections of the fluid.

Preparation of Filtrates.—In all the experiments in this group Berkefeld filtration was started immediately after the material had been collected.

Previous investigations not listed in this paper made it obvious that Berkefeld filtration presented some difficulties. We believed that the filtration should be completed as soon as possible in order to decrease the likelihood of in vitro change of toxic elements.

We found it necessary to dilute the material from the intestine to get it through the Berkefeld filters with a reasonable degree of rapidity. Distilled water was used for the dilution of some of the specimens and isotonic saline solution for the dilution of others. (No difference in toxicity was noted when ether diluent was used.) With five of the specimens a 1:1 dilution was satisfactory, with four a 3:1 dilution and with one a 4:1 dilution. Using these dilutions and carrying on the filtrations at room temperature, we were able to procure each filtrate and inject it into mice at the end of the same day that the original material was obtained from the loop.

Experiments.—Ten dogs were used in this group, the technic for each being the same.

Each was anesthetized with ether; no preliminary medication was used.

The lower 20 to 25 inches (50.5 to 63.5 cm.) of the ileum, to within 3 inches (7.5 cm.) of the ileocecal junction, was identified. The loop was then opened at each end and thoroughly lavaged with running tap water until the return was perfectly clear. (Caution was used in lavaging the loops, as in all other groups, to avoid damage to the loops by excessive pressure of water.) The loop was then stripped dry and the blood supply to it completely ligated. The open bowel ends were closed by ligature, the loop returned to the abdomen and the abdominal wall closed.

The abdomen was reopened without anesthesia in three and one-half to four hours and the reddish, blood-tinged thin to moderately thick fluid collected in a sterile beaker.

Smears were made of pooled and of separate specimens and showed 12 to 20 gram-positive micro-organisms, morphologically Cl. welchii, per oil immersion field. No other micro-organisms were seen.

In one experiment the entire material from the loops of 5 dogs was pooled, diluted 1:1 with distilled water and Berkefeld filtration immediately started. The filtrate was procured in the evening of the same day that the dogs were operated on and was proved sterile by culture and smear. Twelve mice were given single 1 cc. doses of this filtrate (this being equivalent to 8 minims of the original loop fluid by volume), injected intraperitoneally. Eleven of the 12 mice died before 11 o'clock the next day. At autopsy no unusual findings were noted. Some hyperemia of intra-abdominal structures was present in numbers of the animals, but we do not believe any of the mice died from peritonitis. The organs were not sectioned for microscopic study. The mice presented the same lethargic appearance after the injections that had been seen in mice of group II. One mouse recovered.

The loop fluid which could pass through the filter only after 4:1 dilution yielded a filtrate which in an 8 minim dose (equivalent by volume to only 2 minims [0.1 cc.] of the original fluid) was not uniformly lethal to mice. The same was true of the 3:1 dilutions.

CONCLUSIONS FROM GROUP III

Relatively potent toxin is formed in three and one-half to four and one-half hours within a cleansed strangulated loop of ileum in a dog. This toxin is lethal to mice in 8 minim doses when injected intraperitoneally after being sterilized by Berkefeld filtration.

GROUP IV

AN ATTEMPT TO NEUTRALIZE THE TOXIC MATERIAL OBTAINED IN THE FILTRATE OF GROUP III BY MEANS OF B. PERFRINGENS ANTITOXIN

A 10 cc. quantity of the sterile toxic material (the filtrate) from the 1:1 dilutions described in group III was taken for injection into 10 mice. In each of the 10 mice, 8 minims of fresh B. perfringens antitoxin was injected intraperitoneally. Two hours later 1 cc. of the toxic material (filtrate) was injected intraperitoneally into each mouse. Nine of the 10 mice were found dead within twenty-four hours. All injections were made the same day the original fluid had been collected from the loops of the dogs.

Postmorten examination of the mice revealed no findings of note. Peritonitis did not seem to be the cause of death in any. The organs were not sectioned for microscopic study.

CONCLUSIONS FROM GROUP IV

Fresh polyvalent B. perfringens antitoxin did not protect mice against toxin produced in the washed strangulated ilea of dogs.

GROUP V

ATTENUATION OF BACTERIAL PROLIFERATION IN ILEA WITH STRANGULATED BLOOD SUPPLY AND TESTING OF MATERIAL FORMED IN ABSENCE OF BACTERIAL PROLIFERATION

No dogs were used in this group.

In dog 3, series 8A, on Dec. 2, 1938, at 10:45 a. m., all arteries and an occasional vein to the lower 30 inches (76 cm.) of the ileum, beginning just proximal to the

cecum, were ligated. Ether anesthesia was used without preliminary medication. The loop ends were opened and the lumen thoroughly washed with running tap water until the return was clear. The loop was then stripped dry, and about 50 cc. of tincture of merthiolate was introduced into the loop and left there for twenty minutes. Then the loop was washed thoroughly with tap water until the return was entirely clear. After the tincture of merthiolate had remained in the loop for twenty minutes, a small segment of intestine was taken and preserved for microscopic study. (The microscopic report was that the cells and general structure of this membrane did not appear to have been damaged.)

After the loop was thoroughly washed and stripped, its ends were tied off, it was returned to the abdomen and the abdominal wall was closed. At 2:22 p. m. (giving a three hour twenty-three minute specimen) 5 cc. of pinkish red fluid, resembling thin crab meat gumbo, was removed. (This material passed through a small gage needle without difficulty as intraperitoneal injections were made.) The loop was then closed and returned to the abdomen.

(*a*) Four mice were each given an intraperitoneal injection of 8 minims of this 2:22 p. m. specimen. All these mice recovered.

(*b*) At 6:21 p. m. on the same day (giving a seven hour fifty-six minute specimen) about 10 cc. of thick bloody material was collected from the loop without anesthesia or medication. Smears, cultures and injections into mice were made. Six mice were given 8 minims each of this specimen. Five of the mice were found dead the next morning. Autopsies were made, and no evidence of severe peritonitis was present at gross examination. Our records do not show what happened to the remaining mouse. (Since this specimen and that described in the following paragraph were heavily loaded with bacteria, these results were not included in the table.)

(*c*) The loop, after the foregoing specimen had been taken and after it had been stripped, was again returned to the abdomen. The animal was opened again at 9 p. m. of the same day and another specimen taken. Five mice were given 8 minims each of this specimen intraperitoneally. All of these mice were found dead the next morning.

Bacteriologic Slides.—On the 2:22 p. m. (three hour twenty-three minute) specimen the average count was 0.04 per oil immersion field; on the 6:20 p. m. (seven hour twenty-six minute) specimen the average count was 40.4 per oil immersion field. On the 9 p. m. specimen the micro-organisms were too numerous to count; the estimate was 350 per oil immersion field.

From Aug. 13 to 16, 1940, 8 additional dogs were operated on. The loops were thoroughly lavaged as described for previous dogs in this group, stripped dry and treated by instillation of tincture of merthiolate, about 1 cc. to each inch of the 20 to 25 inch loops, the antiseptic being left in the loops exactly twenty minutes. The loops were then thoroughly lavaged with tap water, stripped dry and returned to the abdomens. They were left four to four and one-half hours and then the loop fluid from each animal was collected separately in a sterile beaker. Gram-stained smears were immediately made from the separate specimens. Six of the specimens showed no bacteria in the Gram-stained smear, and one showed 11 gram-positive micro-organisms, morphologically Cl. welchii, per oil immersion field. The latter specimen was discarded.

The results of the intraperitoneal injections made with the material from the 9 dogs of this study are given in the table.

Before the tincture of merthiolate was used in the manner described in group V various antiseptics (aqueous solution of merthiolate [1:1,000], hexylresorcinol [1:1,000], aqueous solution of iodine and 5 per cent aqueous solution of gentian violet) were left in the loops for twenty minutes to five hours and fifty-five minutes after the loops had been washed, in the hope that the bacterial count would be held down. We believed these solutions would be less likely to damage the mucous membrane than tincture of merthiolate. If these antiseptics had prevented bacterial proliferation and at the same time a toxic product had been formed in the degenerating loops, we could possibly have assumed from these experiments alone that toxin was formed from the intestinal wall without the influence of bacterial proliferation. However, with the exception of the aqueous solution of gentian violet the solutions mentioned did not hold down the bacterial proliferation to our satisfaction,

Summary of Experiments in Group V

Dog	Time Loop Fluid Collected After Strangulation	Mice Given Intraperitoneal Injections	Amount, Minims	Mice Recovered and Active Next Morning	Mice That Died Within 24 Hr.
6B	4-4½ hours	5	8	3	2
7B	4-4½ hours	5	8	4	1
8B	4-4½ hours	5	8	4	1
9B	4-4½ hours	3	8	2	1
10B	Discarded				
11B	4-4½ hours	3	8	3	0
12B	4-4½ hours	3	8	3	0
5S8A	2½ hours	5	8	5	0
3S8A	3½ hours	4	8	4	0
Total		33	..	28	5

and consequently these experiments were of no positive value. It was found that 1 cc. of a 1:1,000 aqueous solution of merthiolate injected intraperitoneally does not kill mice, and if it could have been proved that this substance prevented bacterial proliferation, this agent especially would have been of great value in determining the extent of toxin formation in the absence of bacterial proliferation.

It is claimed that the merthiolate in the tincture or in the aqueous solution of merthiolate does not combine with, or in itself chemically alter, protein products. One might wonder whether the alcohol or the acetone which is in the tincture of merthiolate could damage or alter the mucous membrane to the extent that a toxin was not produced whereas it would have been otherwise, even though bacteria had *not* been acting on it. This problem we have not attempted to solve altogether in this series. It is noted in a foregoing paragraph that the pathologist reported that the mucous membrane did not appear on microscopic study to have been damaged by the tincture of merthiolate.

We would call attention again to the work of Trusler, Reeves and Martin, since micro-organisms morphologically Cl. welchii were found almost exclusively in the specimens in our entire study. We believe it highly probable that bacilli of a single specific pathogenic type were not the exclusive factor in the production of the toxins we have studied. It seems probable that proteolytic micro-organisms morphologically Cl. welchii but not necessarily belonging to the specifically recognized pathogenic Welch bacillus types were responsible for the production of toxins through their proteolytic action.

It is possible that toxic protein products can be produced without the proteolytic action of bacteria as tissue degeneration slowly occurs. However, except possibly in newborn infants (and in patients with the high type of obstruction mentioned subsequently) bacteria are always prolifically present in the obstructed intestine. And for practical purposes it seems safe to assume that the toxins in obstructed intestines which are produced most rapidly, frequently and abundantly are the result of the proteolytic action of bacteria on damaged intestinal wall structures. This, of course, does not assume that in high nonstrangulated obstructions in which vomiting and emptying of the intestine occur sufficiently to prevent distention of the latter (this type occurs in a distinct minority) death cannot occur from loss of fluid and electrolyte alone, or that in the absence of proteolytic bacteria the toxins produced by nonproteolytic micro-organisms themselves, as for example streptococci, cannot be absorbed.

CONCLUSIONS FROM GROUP V

Toxic material is formed much less rapidly in the washed strangulated lumens of the ilea of dogs when bacteria are absent than when bacteria are present.

II. THE CHEMICAL NATURE OF THE TOXINS OF INTESTINAL OBSTRUCTION

By J. K. Donaldson, M.D.; E. B. Sive, M.D., and Norman Lewis, M.S.

In July 1931 material was obtained from the loops of three groups of dogs on three different occasions. Twelve dogs were used in the first group, 8 in the second and 4 in the third. In each animal, 20 to 30 inches (50.5 to 76 cm.) of the lower part of the ileum was isolated and the lumen thoroughly lavaged by running tap water until all gross material was removed from the loop and the flow came through perfectly clear. The loop was then stripped as dry as possible and all arteries, veins and lymphatics to the loop were ligated. The bowel

ends were then closed and the loop returned to the abdomen. Ether anesthesia without preliminary medication was used for the first operation on each dog.

Four and a half to five hours later the abdomen was opened without anesthesia or medication and the contents of the loop stripped into a sterile glass container. The dogs were operated on early in the morning and the material obtained was promptly taken by the chemist, and work as related in subsequent paragraphs was started immediately. Caution was taken in each instance to carry the work promptly through to the stage at which, it was felt, alteration of toxin in vitro might be prevented.

In the studies on the three different groups, the steps were essentially the same, and the end results were essentially the same. To avoid reiteration, only the steps and the conclusions reached in the study of the third group are recorded.

Smears on the pooled specimens showed 14 to 25 gram-positive micro-organisms per oil immersion field, which morphologically were Cl. welchii. No other micro-organisms were seen.

CHEMICAL STUDIES ON TOXINS FORMED IN THE PRESENCE OF BACTERIA

A 200 cc. quantity of fluid taken from the loops of the obstructed intestines of the 4 dogs was diluted to one and a half times the original volume with distilled water; it was then centrifuged and the supernatant fluid filtered through paper. The filtered supernatant fluid was labeled solution A.

Effect of Heat on Toxicity of Loop Fluid.—A 30 cc. quantity of solution A was strongly centrifuged and filtered through a Berkefeld filter. This filtrate, free from bacteria, as proved by culture, was divided into two 15 cc. portions, 1a and 1b.

Portion 1a was heated for fifteen minutes in a boiling water bath, the coagulum thrown down in the centrifuge, and the supernatant liquid removed and labeled 1c. The coagulum was extracted with hot water and the extract added to the supernatant fluid, 1c. Portion 1c with the added hot water extract, now called portion 1d, was adjusted to a volume of exactly 15 cc.

Portions 1b and 1d were then compared as to toxicity. They were injected intraperitoneally into seven pairs of mice, each mouse weighing 19 Gm. (plus or minus 2 Gm.). Portion 1b was injected into 7 mice in the following doses, respectively: 4, 8, 12, 16, 20, 24 and 28 minims (0.24, 0.48, 0.73, 0.97, 1.2, 1.4 and 1.7 cc.). All these mice died in less than twelve hours. Portion 1d was injected similarly into 5 mice, in 12, 16, 20, 24 and 28 minim portions, and all these mice recovered. The remainder of 1d was then evaporated to half-volume and injected into 2 mice in 16 and 24 minim portions, corresponding to 32 and 48 minims (1.9 and 2.9 cc.) of the original solution, and these mice died in less than twelve hours.

From these results it appears that (since only 4 minims of 1b were required to cause death and a dose equivalent to 32 minims of 1d was required to produce the same result) the loop fluid was originally about

eight times as toxic to mice as it was after it had been held at 100 C. for fifteen minutes.

It seems that the toxicity of original loop fluid is due to at least two different chemical species; one is water soluble and coagulated by heat (or possibly decomposed without coagulation), while the second is water soluble and not destroyed or coagulated by heat.

Toxic Fractions Precipitated by Alcohol.—A 180 cc. quantity of loop fluid, solution A, was diluted to one and a half times its original volume with distilled water. It was then centrifuged, filtered and poured into 5 volumes of 95 per cent alcohol. The precipitate was filtered off and extracted with 260 cc. of cold distilled water. A 25 cc. quantity of the latter solution was evaporated under diminished pressure to 5 cc. and injected intraperitoneally into 2 mice in 1.5 cc. portions without undue distention of the abdomen. Both mice died in less than twelve hours. The remaining 2 cc. when boiled gave no coagulum, showing the absence of heat-coagulable protein. Then 235 cc. of the water extract was precipitated with 5 volumes of 95 per cent alcohol and allowed to stand overnight. The small white precipitate which formed was thrown down in the centrifuge, and the supernatant liquid was discarded. The precipitate was dried over phosphorus pentoxide in vacuo. It weighed 0.28 Gm. after drying and possessed the following properties:

A quantity weighing 0.28 Gm. dissolved slowly in 9 cc. of water to form a clear brown-tinged solution, which gave a positive Molisch reaction, a weak biuret reaction and no reaction in the Hopkins-Cole, benzaldehyde and Ehrlich diazo tests. It gave no apparent reaction with nitrous acid and did not pass through a collodion membrane. The solution yielded a precipitate on half saturation with ammonium sulfate. This solution injected into 5 mice in 12, 16, 20, 24 and 28 minim portions caused death in less than twelve hours in all the animals. The fatal dose for a 20 Gm. mouse is therefore less than 23 mg.

The Alcoholic Filtrate.—The alcoholic filtrate from precipitation by alcohol of the 235 cc. of original loop fluid mentioned in a foregoing paragraph was evaporated at room temperature under diminished pressure to a thick orange-colored paste, diluted with a small portion of distilled water and again evaporated very nearly to dryness. This procedure was repeated three times to insure complete removal of the alcohol. The volume of the solution was finally adjusted with distilled water to 4 cc. This final solution was a light orange-yellow colloidal one, not cleared by strong centrifuging nor by filtering. Mice receiving 1 cc. doses of this solution intraperitoneally died in four to five minutes, apparently from asphyxia. They ran and leaped about the cage, presenting symptoms of muscular spasm and convulsions. This toxic fraction gave a very strong diazo reaction. The study for histamine in the specimen was done by Kossel's method for the basic amino acids. The alcoholic filtrate was evaporated to small volume, diluted to 50 cc. with distilled water and hot saturated silver sulfate added until an excess of silver was present. The solution was then saturated with powdered barium hydroxide, the precipitate removed and suspended in dilute sulfuric acid, and the silver removed with hydrogen sulfide. The silver sulfide was removed, the filtrate saturated with hot silver sulfate, excess barium carbonate added and the solution boiled. The precipitate which formed on boiling was removed and freed from silver in the usual manner. This filtrate gave a weak diazo reaction but

gave no reaction for histidine by the method of Kapellar and Adler. The positive diazo reaction indicated that histidine was present. (Certain bile acids, however, also will give a positive diazo reaction. The Kapellar-Adler test is specific for histidine but is not extremely sensitive. We believe that histidine was present, but not in sufficient quantity to give the Kapellar-Adler reaction.)

A 50 cc. quantity of the original loop fluid, solution A, was boiled, centrifuged, and filtered and the filtrate poured into 5 volumes of 95 per cent alcohol. The precipitate which formed was filtered off and dissolved in water and again precipitated with alcohol. The precipitate was white, fluffy and larger than that secured from the same amount of loop fluid by the "cold procedure." This precipitate dissolved in water and concentrated was injected into 2 mice in 1.5 cc. portions. Both died in twelve hours or less. The solution gave a positive Molisch reaction and a weak biuret reaction; the Hopkins-Cole and benzaldehyde tests were negative. (This white precipitate is apparently about the same in character as that secured by the cold process.)

STUDIES OF THE CHEMICAL CHARACTER AND TOXICITY OF THE LOOP FLUID FORMED IN THE ABSENCE OF BACTERIA

On Aug. 16, 1940, 4 dogs were anesthetized with ether, and in each approximately 30 inches of the lower part of the ileum, to within 2 inches of the cecum, was isolated. All arteries, veins and lymphatics to each loop were completely closed with ligatures. The loop ends were opened and running tap water directed through the loop without excessive pressure, until the return was completely clear. The loop was then stripped dry and about 1 cc. of tincture of merthiolate per inch of loop instilled. The tincture of merthiolate was left in the loop twenty minutes and was then washed out with running tap water until the return was perfectly clear. The loop was then stripped and the loop ends closed and returned to the abdomen.

In four to four and a half hours the abdomen was reopened without anesthesia or medication and the loop contents collected in a sterile beaker. Smears were made immediately, and in those from 3 specimens no micro-organisms were seen. In that from the fourth specimen there were 12 gram-positive micro-organisms, morphologically Cl. welchii, per oil immersion field. This specimen was discarded from chemical analysis.

As controls, 3 mice were given 8 minim doses of the contents of each of the four loops by intraperitoneal injection. The 3 mice which received doses of the specimen in which the bacteria were seen were all found dead next morning. Of the 9 mice which received doses of the specimens that showed no bacterial content on smear, only 1 died.

The total of the loop material from 2 of the dogs which showed no bacteria on smear was not treated with heat. It was diluted 1 : 1, promptly centrifuged and precipitated with alcohol exactly as outlined in the section entitled "Chemical Studies on Toxins Formed in the

Presence of Bacteria" (p. 831). The same chemical analyses and procedures as outlined there were used in the study of this specimen, and the same results were obtained with the following notable exceptions:

The Alcoholic Filtrate.—This term has the same connotation here as in connection with the chemical studies of toxins formed in the presence of bacteria (p. 832). Ehrlich's diazo test was absolutely negative on this alcoholic filtrate. This was conclusive evidence that no histamine was present.

The alcohol-soluble product from the intestinal loops of the 2 dogs was adjusted with distilled water to a final volume of 30 minims. A 1 cc. and a 14 minim (0.85 cc.) dose of this slightly muddy amber-colored solution from which all alcohol had been removed were injected intraperitoneally into 2 mice, respectively, on August 19.

About two minutes after the injection of the 14 minim dose, the mouse presented some labored respiration, seemingly a general tightening of all muscles of the body and some increase in excitability. The reaction was similar to, perhaps, but much milder than, the reactions seen in the animals which had previously been given an alcohol-soluble toxic fraction as mentioned in the previous section. The injection was made at 5:50 p. m. At 6:15 p. m. the mouse was leaning to the left side and moved gradually in a circle to the right about the cage. This reaction persisted for thirty minutes or more. At 6:30 p. m. the animal was quite ill and lethargic. The next morning (August 20) at 9:30 a. m. the animal was excitable, and when the cage was tapped lightly it went into a general spasm with only mild convulsions and appeared dead for a few seconds but then became active again. Both left extremities continued to be partially paralyzed. The animal was found dead at 8 a. m., August 21.

The second mouse was given the 1 cc. dose of the fraction at 5:45 p. m. on August 19. The animal showed some slightly labored respiration and moderately increased excitability. At 6:15 p. m. it was rather quiet, and at 6:25 p. m., after two or three very labored respiratory cycles, it died rather quietly. This animal showed no manifestations of paralysis or convulsions.

Fractions Precipitated by Alcohol.—This term likewise is synonymous with that in the section on toxins formed in the presence of bacteria. The feathery-like white alcoholic precipitate which was collected and treated by the method outlined in that section (p. 831) was isolated.

The feathery-like precipitate to alcohol was the same in appearance as the product obtained and described in that section. However, only 0.06 Gm. of the material was obtained. This was only a fifth to a third of the total amount which had been obtained in the same experiment of

that section as compared proportionally to the amount collected from 2 dogs in that experiment. This material was dissolved in distilled water.

A 1.5 cc. dose of this solution was injected into each of 4 mice, this dose giving 0.018 Gm. of the isolated product. (This was approximately the same dose as used in the injection of the product which had been formed in the presence of bacteria, as set forth in the previous section.)

The solution was injected into mice on August 19. None of these mice died. None appeared especially ill after the injections. All were active the next morning.

COMMENT

The numerous and repeated observations made during the studies outlined in parts I and II of this paper warrant some definite conclusions. Certainly very toxic substances are formed from the tissues of the wall of the strangulated small intestine in the presence of bacteria, irrespective of gross substances normally found within the lumen of the intestinal tract. These toxic substances are formed early, being present in quite appreciable quantities within three to four hours after strangulation has occurred. No studies relative to the mechanics of absorption of such substances have been made here, but work of previous investigators and of the senior author (J. K. D.), together with a practical consideration of the problem of obstruction in the human being, leaves no doubt that such substances may be absorbed into the general system.

Previous workers have concluded that bacteria are essential to the production of toxins from the intestinal wall itself, and though we cannot go so far as to use the word "essential," our studies certainly confirm the opinion that if bacteria are not essential to the production of such toxins, they nevertheless enhance the rapidity of toxin formation considerably. B. perfringens antitoxin (Lilly) does not neutralize the toxic substances.

A most consistent reaction was produced in our animals by an injected toxin which caused lethargy and evident general depression of the animal, with death in about twenty-four hours. Studies not described in this paper, which were made on rats with toxic but not fatal doses of our products, have occasionally demonstrated paralysis of some of the motor nerves (and possibly degeneration of the optic nerve, though this probably is not established with certainty).

The second type of reaction which occurred in our animals, from another isolated toxic fraction, was death occurring within one to five minutes after intraperitoneal injection of the toxin, preceded by markedly labored respiration, marked excitement and apparently asphyxia, these pharmacologic reactions being similar to those produced by histamine.

The toxic fraction causing the latter reaction is found in much smaller quantities than the toxin producing the slower reaction.

Protein chemistry is a specialty within itself, there being probably thousands of protein compounds which have not been accurately identified structurally. Any chemical attempt to identify most protein compounds structurally must in itself initially alter many of the compounds in such a way that their exact structural recapitulation becomes most difficult after the first step of a chemical study.

We are not justified in assuming from our work that we have made accurate identifications of our toxic substances. We should like to believe the substances are split products of protein degeneration, the degeneration being enhanced by proteolytic bacteria. Other workers have asserted that the toxic substances are proteoses. Certain parts of our chemical studies indicate that primary and secondary proteoses are the toxic substances. And yet though our work has been as extensive as that of some investigators who have claimed identification of proteoses, we do not feel justified in making the broad assertion that proteoses are the primary toxic factors. In fact a toxin, these studies indicate, belonging chemically to the class of carbohydrates has been repeatedly identified by the consistent appearance of the positive Molisch reaction. So, though we are justified in the conclusions that follow, more intensive study on toxins procured by our method or one similar, a method which does isolate in the beginning very markedly toxic products, which are formed early in the strangulating intestinal wall, is indicated before physicians can accept the statement that a positive identification of any toxin has been made.

Clinically, in the majority of cases of fatal obstruction in man, there is interference with the blood supply to the intestinal wall either directly by strangulation or secondarily by distention. Therefore every effort should be made to determine as accurately as possible the exact nature of the toxins produced by interference with the blood supply in the hope that, as a subsequent step, some neutralizing agent can be found.

SUMMARY OF PARTS I AND II WITH CONCLUSIONS

Thin, relatively clear, untreated, nonsterile, fresh, normal ileac secretion from dogs is not lethal to mice when injected in relatively large doses (8 minims) intraperitoneally, provided the bacterial content of the fluid is low (arbitrarily below 8 to 10 micro-organisms per oil immersion field).

As demonstrated in part I, the sterile filtrate of loop fluid from the walls of degenerating ilea of dogs becomes lethal to mice in two and a half hours or less after strangulation of the arterial blood supply to the loops.

Our principal toxic substances injected intraperitoneally into mice in about minimum lethal doses gave a consistently characteristic reaction. The reaction is one of lethargy and evident general depression, with death occurring in twenty-four hours or less after the injection.

Two fractions are obtained from the principal substances giving the toxic reaction just described, and each of the two fractions causes the same type of depressive reaction when injected into mice. One of the fractions is water soluble, is coagulated or destroyed by heat and contains roughly 85 per cent of the total toxicity of the whole of the fresh substance obtained from the strangulated intestinal wall. The second toxic fraction is water soluble and is not destroyed by heat.

Another toxic fraction is soluble in alcohol and water, is not destroyed by heat, is produced in small quantities and gives a rapidly fatal death when injected into a mouse. Death occurs in one to five minutes after the injection and is preceded by excitement, muscle spasm and rigidity and apparent asphyxia, a reaction very similar to, if not exactly, that produced by histamine. We believe this toxic substance is histamine or a very similar substance.

Practically all the toxic substances that we isolated were produced in the presence of bacteria. Only a small amount of a toxic substance soluble in alcohol and water (not histamine) was isolated from strangulated intestine in the absence of bacteria. This small bit of substance was lethal to mice, however, though producing death less rapidly than the histamine or histamine-like fraction.

Polyvalent B. perfringens antitoxin does not counteract the toxins we produced.

One of the main reasons why so much confusion remains regarding the problem of intestinal obstruction is that research workers have generalized too broadly on the secondary factors in the morbid picture of intestinal obstruction.

It has been repeatedly proved that nothing will save the patient unless the strangulated intestinal tissue is removed when this is a factor in obstruction. It has also been accepted that death of intestinal tissue occurs not only from direct strangulation but from distention alone.

We followed a method of experimentation which procures fresh toxic substances from a strangulated intestinal wall. We have demonstrated that these principal toxic substances are not found by our method of experimentation in the absence of bacteria but are produced quite rapidly (within two to four hours) in appreciable quantities in the presence of proliferating bacteria.

Despite rather extensive investigation, the difficulties of chemical analysis of protein compounds make us reluctant to identify the principal substances as proteoses, though some of our tests indicate that they are

primary and secondary proteoses. However, a substance giving a positive reaction in the Molisch test for carbohydrates is present.

Repeated investigations with the toxic substances obtained by our method or similar methods should be carried out by investigators in an attempt to identify more accurately the toxins which we have found by the methods described. If these toxins could be more accurately identified, it might be possible to find a neutralizing agent for them and thereby make an important contribution to the therapy of obstruction.

Prof. Howard Reynolds, of the University of Arkansas, reviewed the results of the chemical studies in the absence of Mr. Lewis. Drs. J. G. Wahlin, C. H. McDonald, Paul L. Day, of the departments of bacteriology, physiology and pharmacology, and physiological chemistry, respectively, gave helpful suggestions. Eli Lilly & Company (at the request of Dr. E. G. Stewart and Mr. J. E. Hoffmeister) supplied the freshly prepared B. perfringens antitoxin and the solutions of merthiolate used in the investigation.

HODGKIN'S DISEASE

REVIEW OF FIFTY-FOUR CASES

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Since Thomas Hodgkin's [1] report in 1832 of 7 cases in which there was presented a syndrome of swelling of the superficial lymph nodes and enlargement of the liver and spleen with anemia, followed by cachexia and death, many similar reports have appeared in the literature. Hodgkin did not affix a name to the disease; this was left to Wilks,[2] who in 1865 recorded 15 similar cases and applied the name Hodgkin's disease. Not all of Hodgkin's original 7 cases are considered to present true examples of the disease. Wilks,[2] Reed,[3] Halsted [4] and Fox [5] expressed the opinion that only 2 to 4 of the cases offer true examples of the disease process, the others being cases of tuberculosis, syphilis and leukemia.

The monumental work of Sternberg [6] (1898) and Reed [3] (1902) did much to clarify the histologic picture and pathologic behavior of the disease. Both gave excellent descriptions and appended good drawings and sketches, placing particular emphasis on the occurrence of the large giant endothelial cells which carry their names. Wallhauser [7] found about fifty synonyms for the disease, indicating considerable confusion as to classification and causation, although the histologic and the pathologic pictures have remained clear for forty years.

The theories of causation have varied from an infectious to a neoplastic basis, with many holding to an entity midway between.

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1. Hodgkin, T.: Med.-Chir. Tr., London **17**:68, 1832; reprinted, M. Classics **1**:742, 1937.
2. Wilks, W.: Guy's Hosp. Rep. **9**:56, 1865.
3. Reed, D.: Bull. Johns Hopkins Hosp. **10**:133, 1902.
4. Halsted, W. S., cited by Jones, G. W.: Ann. M. Hist. **2**:471, 1940.
5. Fox, H.: Guy's Hosp. Rep. **86**:11, 1936.
6. Sternberg, C.: Ztschr. f. Heilk. **19**:21, 1898.
7. Wallhauser, A.: Hodgkin's Disease, Arch. Path. **16**:522 (Oct.) 1933.

Sternberg [6] expressed the belief that the disease is an atypical form of tuberculosis, although this was opposed vigorously by Reed,[3] who maintained the process is an infective granuloma of unknown cause. Fraenkel and Much [8] (1910) and Bunting and Yates [9] (1913) reported that they found specific causative organisms.

Gordon [10] in 1932 described a test, positive in 70 per cent of the cases, which consisted of intracerebral injection of a broth suspension of diseased lymph nodes into rabbits and guinea pigs. A syndrome consisting of spastic paralysis, ataxia, retraction of the head, fits and loss of weight was produced. He was convinced that a virus was responsible for the disease. In 1938, four different workers [11] showed that the eosinophils in tissue affected by Hodgkin's disease were responsible for the encephalitic reaction of the animals and that the same reaction can be produced by other tissues containing eosinophils. The Gordon test is a valuable confirmatory test when accompanied by histologic examination, as shown recently by Steiner,[12] who found the test positive in 73.9 per cent of 299 recorded cases of histologically proved Hodgkin's disease and falsely positive in only 1.77 per cent of 452 control cases.

In 1939 Parsons and Poston [13] reported a group of 4 cases of human brucellosis in which the histologic study of lymph nodes and autopsy material revealed the characteristics of typical Hodgkin's disease. Recently at the same hospital Forbus and Gunter [14] studied autopsy material from 4 additional cases of typical Hodgkin's disease, with recovery of the Brucella organism in all. Poston and Parsons [15] reported cultures of Brucella from the lymph nodes of 10 of 19 patients with Hodgkin's disease.

The present paper analyzes 54 cases of histologically proved cases of Hodgkin's disease observed at the University of Virginia Hospital in the past fifteen years. Biopsy was performed in 51 cases and autopsy

8. Fraenkel, E., and Much, H.: Ztschr. f. Hyg. u. Infektionskr. **67**:159, 1910.

9. Bunting, C. H., and Yates, J. L.: Cultural Results in Hodgkin's Disease, Arch. Int. Med. **12**:236 (Aug.) 1913.

10. Gordon, M. H.: Rose Research on Lymphadenoma, Bristol, John Wright & Sons, Ltd., 1932.

11. Edward, D. S.: Lancet **1**:936, 1938. King, D. P.: St. Thomas's Hosp. Rep. **3**:68, 1938. McNaught, J. B.: Gordon Test for Hodgkin's Disease: Reaction to Eosinophils, J. A. M. A. **111**:1281 (Oct. 1) 1938. Turner, J. C.; Jackson, H., Jr., and Parker, F.: Am. J. M. Sc. **195**:27, 1938.

12. Steiner, P. E.: Reliability and Significance of Gordon Test in Hodgkin's Disease, Arch. Path. **31**:1 (Jan.) 1941.

13. Parsons, P. B., and Poston, M. A.: South. M. J. **32**:7, 1939.

14. Forbus, W. D., and Gunter, J. U.: South. M. J. **34**:376, 1941.

15. Poston, M. A., and Parsons, P. B.: J. Infect. Dis. **66**:86, 1940.

in 4. About 20 other cases were not included because the histologic changes were inconclusive or the diagnosis was merely clinical. One case in which Hodgkin's disease was diagnosed on biopsy of a cervical lymph node is omitted; this will be reported separately,[16] as the patient died three months later of generalized torulosis.

INCIDENCE

Race.—Hodgkin's disease has been reported to attack every race and nearly all nationalities. The reports of cases in America indicate that the distribution has been predominantly among the white and American born. Goldman[17] reported an incidence of 6.6 per cent Negroes in a group of 212 patients with Hodgkin's disease.

In our series the condition occurred in 45 white persons (83.3 per cent) and 9 Negroes (16.7 per cent). Over a period of many years the average admission rate of Negroes at this hospital has been 15.6 per cent.

Sex.—The disease is more prevalent in men than in women. Wallhauser[7] collected 1,447 cases from the literature and found the incidence to be 70 per cent in men and 30 per cent in women.

In our group there were 32 men (59.3 per cent) and 22 women (40.7 per cent).

Age.—Hodgkin's disease may occur at any age. Smith[18] collected 5 cases in which the onset was before the sixth month of age. A number have been recorded in which the condition developed in the seventh and eighth decades of life. In the greatest number of cases the onset occurred in the third decade of life.

The youngest patient in our series was 4 and the oldest 70. The greatest number of the patients were in the third decade of life; the incidence of the disease was fairly well distributed over the other decades except the sixth, in which it was low, and the seventh, in which it was higher than in any except the third (chart).

PREDISPOSING FACTORS AND POSSIBLE CAUSES

There were no demonstrable predisposing factors in any of the cases studied. Heredity, environment, occupation and food appeared to play no important part. The majority of the patients were ward patients, but there were 2 physicians' wives and 1 hospital intern in

16. Morton, C. B.; Derrick, W. A., and Burger, R. E.: Torula Infection: A Review and Report of Three Cases, to be published.

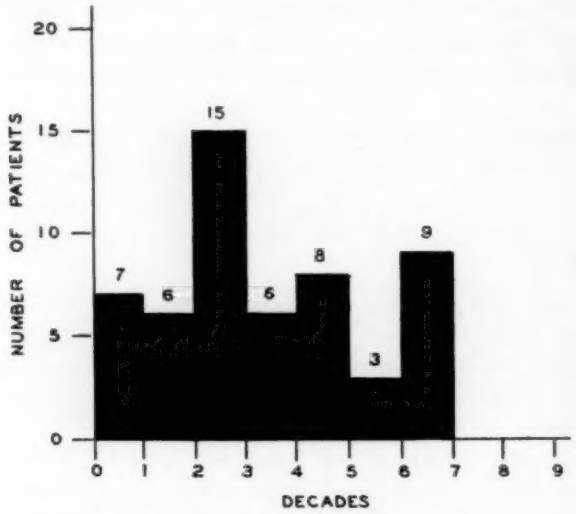
17. Goldman, L. B.: Hodgkin's Disease: Analysis of Two Hundred and Twelve Cases, J. A. M. A. **114**:1611 (April 27) 1940.

18. Smith, C. A.: J. Pediat. **4**:12, 1934.

the group. There was no familial history of Hodgkin's disease. McHeffey and Peterson [19] reported the occurrence of Hodgkin's disease in 2 brothers almost simultaneously.

Roentgenograms of the chest in 3 cases revealed scarring and calcification consistent with old healed tuberculosis; in 3 additional cases there was suspicion of activity, and in 1 case there was death from concomitant pulmonary and miliary tuberculosis and Hodgkin's disease. Thus in 12.9 per cent of the cases there was healed or active tuberculosis.

Of the 54 cases, cultures of the blood were made in 3 and of the lymph nodes in 2. In 1 case the culture of the blood was positive for Brucella.



Age incidence in 54 cases of Hodgkin's disease.

CHIEF COMPLAINTS AND SYMPTOMS

Swelling of the glands of the neck, weakness, fatigue, loss of weight, cough, dyspnea and backache were the commonest complaints on admission to the hospital. Table 1*A* records the chief complaint and table 1*B* the symptoms present on admission in 44 cases; in 10 cases there were no symptoms except the swelling of glands.

The average time between the onset of symptoms and entry into the hospital in 52 cases was ten and one-half months. There was no record of the duration of the disease before admission in 2 cases.

19. McHeffey, G. J., and Peterson, R. F.: Hodgkin's Disease Occurring Simultaneously in Two Brothers, J. A. M. A. **102**:521 (Feb. 17) 1934.

TABLE 1.—*Chief Complaints and Symptoms in Cases of Hodgkin's Disease*

A. The Chief Complaint That Brought 54 Patients to the Hospital			B. The Most Common Symptoms Prior to Hospitalization in 44 Cases (In 10 Cases There Were No Symptoms)		
Complaint	Patients	Per Cent	Common Symptoms	Cases	Per Cent
Swelling of the glands of the neck	31	57.4	Weakness	26	48.2
Fatigue and weakness	5	9.3	Loss of weight	19	35.2
Pain in the back and the legs	5	9.3	Cough	13	24.1
Cough, dyspnea and sore throat	3	5.6	Fatigue	9	16.6
Abdominal pain	3	5.6	Anorexia	8	14.8
Mass in the abdomen	2	3.7	Pain in the back and the legs	8	14.8
Generalized superficial glandular enlargement	1	1.8	Malaise	7	12.9
Enlargement of the inguinal glands	1	1.8	Nervousness	6	11.1
Pain in the eyes and head	1	1.8	Edema	6	11.1
Cutaneous lesions	1	1.8	Dyspnea	5	9.3
Tuberculosis	1	1.8	Fever	5	9.3
			Headache	4	7.4
			Abdominal pain	4	7.4
			Nausea and vomiting	3	5.6
			Night sweats	2	3.7
			Sore throat	2	3.7
			Pain in the neck	2	3.7
			Pruritus	2	3.7

CLINICALLY OBSERVED LOCALIZATION

Although the disease is usually generalized, with widespread involvement of the reticuloendothelial system, definite areas of localization are observed clinically. A characteristic of the disease in the early stages is that unilateral lymphatic areas are attacked more frequently than symmetric areas. The lymph nodes of the neck were involved first in two thirds of the cases. Table *2A* gives the regions first involved in this group, determined by palpation, roentgenograms and surgical exploration. Table *2B* gives the frequencies of involvement of lymph nodes, tissues and organs during the course of the disease.

Mediastinum.—Involvement of the mediastinum, as evidenced in roentgenograms by widening, nodular protrusions of enlarged glands and actual infiltration of the lungs, was present in 55.5 per cent of the cases. In 2 cases the mediastinal nodes were apparently the first of the body structures to be involved. There was involvement of mediastinal nodes in all 4 of the patients who came to autopsy.

Stomach.—Sherman [20] in 1938 collected 75 cases of Hodgkin's disease in the gastrointestinal tract from the literature, and in about a third of these cases there was involvement of the stomach.

The stomach and regional lymph nodes were involved in 2 cases of our series. In each instance a roentgenogram revealed a large filling defect in the stomach, and at exploration a large mass was found in the stomach, with involvement of regional lymph nodes. These were thought to be cases of inoperable carcinoma till biopsy of the regional nodes revealed Hodgkin's disease.

Spleen.—During the course of the disease the spleen was observed clinically to be enlarged in 33.3 per cent of the cases. Of the 4 patients who came to autopsy, 3 had involvement of the spleen, and 2 of these had palpably enlarged organs.

Desjardins and Ford [21] (1923) noted splenomegaly in only 14.9 per cent of 135 cases. Boyd [22] stated that 75 per cent of the cases show splenomegaly.

Liver.—The liver was palpable in 20 (37 per cent) of the cases. This is somewhat lower than the 60 per cent given by Ziegler [23] and

20. Sherman, E. D.: Gastro-Intestinal Manifestations of Lymphogranulomatosis (Hodgkin's Disease), Arch. Int. Med. **61**:60 (Jan.) 1938.

21. Desjardins, A. V., and Ford, F. A.: Hodgkin's Disease and Lymphosarcoma, J. A. M. A. **81**:925 (Sept. 15) 1923.

22. Boyd, W.: The Pathology of Internal Diseases, Philadelphia, Lea & Febiger, 1934.

23. Ziegler, K.: Die Hodgkinsche Krankheit, Jena, Gustav Fischer, 1911.

TABLE 2.—*Cases in Which Involvement of Certain Organs Was Shown*

A. Region First Involved			B. Region Involved at Some Stage of the Disease		
Organ or Nodes	Cases	Per Cent	Organ or Nodes	Cases	Per Cent
Left cervical nodes	15	27.8	Left cervical nodes	44	81.5
Right cervical nodes	14	25.9	Right cervical nodes	37	68.5
Cervical nodes on both sides	7	12.9	Axillary nodes	27	50.0
Inguinal nodes	6	11.1	Inguinal nodes	20	37.0
Axillary nodes	3	5.6	Epitrochlear nodes	1	1.8
Abdominal nodes, liver and spleen	3	5.6	Mediastinum	30	55.5
Generalized superficial glands	2	3.7	Liver	20	37.0
Mediastinum	2	3.7	Spleen	19	35.2
Stomach and regional nodes	2	3.7	Abdominal nodes	8	14.8
			Stomach and regional nodes	2	3.7
			Bone	4	7.4
			Skin	2	3.7
			Eye and retrobulbar tissues	2	3.7

the 50 per cent given by Boyd.[22] The liver was involved in 2 of the 4 cases in which there was an autopsy and in 1 in which surgical exploration was done. There was clinical icterus in 2 (3.7 per cent) of the cases; this was in agreement with 4.2 per cent in Goldman's[17] 212 cases.

Skin.—Cutaneous involvement was proved histologically in 2 cases. In the first it was associated with generalized superficial glandular enlargement; in the second, with involvement of the liver proved by biopsy. Puritus was present during the course of the disease in 10 (18.5 per cent) of the cases.

Bone.—In 4 of the cases (7.4 per cent) there was roentgen evidence of osseous involvement. Goldman[17] reported osseous involvement in 6.6 per cent of 212 cases and Craver and Copeland[24] in 15.7 per cent of 172 cases. The bones involved in our series were more commonly the vertebrae, less often the pelvic bones, sacrum and ribs. Biopsy of involved bone of 2 of the patients showed tissue typically affected by Hodgkin's disease. Three other patients complained of moderately severe pain in the back and hips at some time during the course of the disease, but roentgenograms were never taken.

BLOOD PICTURE

Opinions as to the blood picture in Hodgkin's disease differ widely. Bunting[25] emphasized certain changes in the blood count and blood smear, but these are variable. Steadily progressive anemia of the hypochromic type is usually found. In this series 32 (59.3 per cent) patients had a leukocyte count above 8,000. The two highest leukocyte counts were 68,300 and 54,000, with polymorphonuclears predominant; eosinophils were not present in the blood smear in the first instance and were 2 per cent in the second. In both the leukocytosis was accompanied by rather severe secondary anemia. Both the patients had superficial glandular enlargement plus bony involvement. The leukocyte count of 1 patient receiving no treatment was 2,600. Five patients receiving roentgen therapy had their previously normal leukocyte counts depressed below 4,000. The leukocyte counts of the remainder of the patients were within the normal range.

Eosinophilia has long been stressed as a characteristic finding. Goldman[17] and Baker and Mann[26] observed eosinophilia in 20 per cent of their cases. In our series there was eosinophilia (5 per cent

24. Craver, L. F., and Copeland, N. M.: Changes in Bone in Hodgkin's Granuloma, Arch. Surg. **28**:1062 (June) 1934.

25. Bunting, C. H.: Bull. Johns Hopkins Hosp. **25**:173, 1914.

26. Baker, C., and Mann, W. N.: Guy's Hosp. Rep. **89**:83, 1939.

or more) in 20.3 per cent of the cases. The highest was 25 per cent, in the case of Hodgkin's disease of the skin associated with superficial glandular disease.

OCCURRENCE OF FEVER

In 1887 Pel [27] and Ebstein [28] described periodic bouts of fever with remissions in the disease process. Of the 54 patients in our series, all but 5, whose disease was in an early stage, were pyrexic when observed. A continued or swinging pyrexia with temperatures from 100 to 104 F. was much more common than the classic Pel-Ebstein variety, which occurred in only 8 (14.8 per cent) of the patients under observation.

DURATION OF LIFE

Hodgkin's disease may be rapidly fatal or slowly progressive. Two of the patients whose disease ran the shorter course lived about three months after the onset of symptoms; the patient who lived longest died eight years, eight months after the onset. The average duration of life of 41 patients followed up and known to be dead was twenty-six months, dating from the onset of symptoms. Four patients are thought to be dead, but a follow-up could not be obtained. Nine patients known to be alive have been living an average of twenty-nine and five-tenths months at the time of writing. In Goldman's [17] 212 cases the average duration of life was about thirty-two months; in Baker and Mann's [26] 65 cases it was about eighteen months. Craver [29] reported periods of survival of five years or more in 12 per cent of 125 proved cases of Hodgkin's disease. In our series 3 patients (5.6 per cent) are known to have lived longer than five years.

SECONDARY CAUSES OF DEATH

In 28 of the known fatal cases the mode of death is known and is given in table 3.

Terminal exhaustion, anemia and pyrexia were mentioned most often, being present in 21 cases.

Death due to respiratory failure with signs of pulmonary disease or mediastinal compression occurred in 6 cases. One patient died on the operating table shortly after an attempt to decompress the mediastinum because of marked respiratory difficulty.

In 1 case there were concomitant Hodgkin's disease and pulmonary and miliary tuberculosis.

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27. Pel, P. K.: Berl. klin. Wchnschr. **24**:644, 1887.
28. Ebstein, W.: Berl. klin. Wchnschr. **24**:565, 1887.
29. Craver, L. F.: Am. J. M. Sc. **188**:609, 1934.

In many there was overlapping of the terminal symptoms, and it was rather difficult to select the cause of death.

RESULTS OF TREATMENT

The methods of treatment in this series of cases are given in table 4. The larger number of the patients (41) were given roentgen therapy alone to the involved areas. A few had surgical or radium treatment alone; 2 had combined surgical and roentgen therapy, and 5 received no treatment.

In the group known to be dead the average duration of life was much greater in those receiving treatment, regardless of the type of

TABLE 3.—*Mode of Death in Twenty-Eight Cases of Hodgkin's Disease*

Type	Cases	Per Cent
Respiratory failure	6	21.4
Exhaustion, anemia and pyrexia	21	75.0
Miliary tuberculosis	1	3.6

TABLE 4.—*Results of Treatment* *

	Patients (41) Known to Have Died		Patients (9) Still Alive	
Type of Therapy	Patients	Average Length of Life (Mo.)	Patients	Average Living Time at Time of Writing (Mo.)
Roentgen alone	30	28.1	9	29.5
Surgical alone	3	28.2	..	....
Radium alone	1	30.0	..	....
No treatment	5	10.4	..	....

* Of the patients who were not followed up, 2 received roentgen therapy alone and 2 combined surgical and roentgen therapy.

therapy, than in those not receiving treatment. Those receiving some form of therapy lived twenty-eight to thirty months; those not receiving treatment lived only ten and four-tenths months.

In 9 living patients receiving repeated irradiation of involved tissues the duration of life at the time of writing was already twenty-nine and five-tenths months. Roentgen irradiation of the entire lymphatic system has not been tried at this hospital. Blood transfusions and general therapeutic measures have been valuable adjuvants in building up the patients.

Most roentgen therapeutists use repeated local application of irradiation. Jacox, Peirce and Hildreth [30] in surveying the clinical results

30. Jacox, H. W.; Peirce, C. B., and Hildreth, R. C.: Am. J. Roentgenol. **36**:165, 1936.

of this form of treatment in 161 cases of Hodgkin's disease over a decade, were convinced that roentgen therapy induced definite extension of life and that systemic irradiation was proving more effectual in prolonging life than repeated local irradiation.

Regardless of the type of therapy, Hodgkin's disease has proved an almost universally fatal malady in the proved cases. There are a few isolated reported cures, but as to most of these there is a question of correct diagnosis or of adequate follow-up. A few cases have been reported in which the patient lived twenty years or more, and Jackson [31] recorded a case in which there was recurrence of nodes removed surgically after a lapse of twenty-six years.

SUMMARY

We have analyzed 54 cases of histologically proved Hodgkin's disease seen at the University of Virginia Hospital in the past fifteen years. In discussing the clinical features, we have compared our figures with others occurring in the literature.

No data relating to causation are presented. In 1 case among 3 studied by culture of the blood, Brucella was isolated.

Enlargement of the cervical glands is commonly the first sign and is followed later in most instances by involvement of superficial and mediastinal nodes, accompanied by swinging or sustained pyrexia, usually not of the Pel-Ebstein type.

The average time of survival from the onset of the first symptom was twenty-six months. Treatment in most cases consisted of repeated roentgen irradiation of involved tissues aided with blood transfusions and general therapeutic measures. Treated patients have on the average survived nearly three times as long as untreated patients.

Dr. W. Ansell Derrick, of the department of pathology of the University of Virginia, assisted in reviewing the histologic slides.

31. Jackson, H., Jr.: M. Clin. North America **21**:361, 1937.

PREOPERATIVE MANAGEMENT OF GASTROJEJUNOCOLIC FISTULA

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The immediate mortality rate after surgical intervention in the treatment of well developed gastrocolic fistula is disturbingly high, and yet the prognosis for the disease if treated by medical means alone is exceedingly poor. Nearly all patients treated medically die of progressive inanition, avitaminosis or intercurrent infection. Verbrugge [1] reported a series of 20 cases in which 5 patients died after operation; the mortality rate was thus 25 per cent. Loewy [2] collected reports of 63 cases; the operative mortality rate in this group was 27 per cent. Allen [3] reported 8 cases with 2 deaths; Lahey and Swinton [4] reported an immediate mortality rate of 63 per cent in 8 cases and Rife [5] a mortality rate of 20 per cent in 14 cases. A high mortality rate seems to accompany any type of operation performed in one stage, regardless of the technic employed or the quality of the postoperative management.

The first report of a spontaneous communication between the stomach and the colon was made by Haller [6] in 1755. Prior to 1903, when Czerny [2] reported the first case of gastrojejunocolic fistula after gastroenterostomy, in most of the 70 cases reported the anomaly was caused by carcinoma of the stomach or the colon. Since that time the increasing use of gastroenterostomy in the treatment of duodenal ulcer has resulted in the establishment of a communication from the stomach to the jejunum and colon in many cases. When such a fistula occurs now, it is usually presupposed that gastroenterostomy has been performed —in most cases, years before for benign duodenal ulcer—and that an eroding, adherent gastrojejunal ulcer developed. Such a communication

From the Division of Surgery, Mayo Clinic.

1. Verbrugge, J.: Gastrojejunocolic Fistulas, Arch. Surg. **11**:790-808 (Nov.) 1925.

2. Cited by Pfeiffer and Kent.[11]

3. Allen, A. W.: An Aseptic Technic Applicable to Gastrojejunocolic Fistula, Surgery **1**:338-348 (March) 1937.

4. Lahey, F. H., and Swinton, N. W.: Gastrojejunal Ulcer and Gastrojejunocolic Fistula, Surg., Gynec. & Obst. **61**:599-612 (Nov.) 1935.

5. Rife, C. S.: Gastrojejunocolic Fistula, Am. J. Surg. **40**:73-88 (April) 1938.

6. Haller, cited by Tynes, A. L., and Cole, F. L.: Gastrojejunocolic Fistula with Report of Three Cases, Mil. Surgeon **86**:113-121 (Feb.) 1940.

after gastroenterostomy for gastric ulcer is rare and seldom occurs in women. Gastrojejunocolic fistula apparently occurs in 0.1 to 0.2 per cent of the cases in which gastroenterostomy is performed and in about 10 per cent of the cases in which gastrojejunal ulcer develops.

PURPOSE AND MATERIAL OF STUDY

It is the purpose of this study to present a review of 49 consecutive cases of well developed gastrojejunocolic fistula in which operation was performed at the Mayo Clinic from 1930 to 1939, inclusive. Cases of so-called impending fistula are not included. All operations were performed in one stage, but many different types of corrective measures were used; these have been described by Walters and Clagett.[7] Besides the one stage operation, the only other constant factor in these cases was the preoperative management and preparation of the patient. Emphasis will therefore be placed on the preoperative management and the effect of this on the immediate operative mortality.

Factors which enter into the prevention of such fistulas will not be mentioned, except to emphasize that a great part of the rationale of preoperative management of fistula is based on the knowledge that the disease is a manifestation of a long-standing debilitating process. Furthermore, most of the patients are not cooperative with medical treatment, as evidenced by the fact that in most of the cases reported here the duodenal ulcer, then the gastrojejunal lesion and, finally, the gastrocolic fistula, developed while the patient was receiving medical care. It is apparent also that the inanition and avitaminosis resulting from such lesions may be productive of postoperative peritonitis, tetany and pneumonia.

DATA ON PATIENTS

None of the 49 patients of this series were women. All patients had undergone gastroenterostomy for duodenal ulcer. In 40 cases posterior gastroenterostomy alone was the primary procedure. In 8 cases, previous acute perforation of a duodenal ulcer had occurred; the opening was closed, and posterior gastroenterostomy was performed then or later. The duodenal ulcer of 1 patient had been excised and posterior gastroenterostomy performed; the usual symptoms of duodenal ulcer had occurred. Of the 49 patients, only 7 had cooperated in their medical treatment; the rest had been listed as poorly cooperative or noncooperative.

In 14 cases in this series, further operations had been performed on the stomach after the initial gastrojejunostomy and prior to the formation of the fistula. These operations, which were usually made necessary by the formation of an anastomotic ulcer, consisted preponderantly of

7. Walters, W., and Clagett, O. T.: Gastrojejunocolic Ulcer and Fistula, Am. J. Surg. **46**:94-102 (Oct.) 1939.

some type of plastic or short-circuiting procedure. The operations were almost always futile, unless some type of gastric resection was performed. Even then the fistula ultimately formed. Whether early gastric resection would have forestalled the final penetrating ulcer cannot be said definitely. One patient had undergone four such intervening operations. Two years after the initial gastrojejunostomy, an enteroanastomosis for correction of a malfunctioning stoma was carried out. A year later an exclusion operation of the Devine type was performed in an attempt to control the anastomotic ulcer. In five months the gastrojejunal ulcer was excised without changing the continuity of the gastrointestinal tract. Nine years later a Billroth I operation of the von Haberer type was performed. Two patients required three such intervening operations; 4 had two, and the remaining 7 patients had one operation between the gastroenterostomy and the final operation.

The necessity for repairing the gastrojejunocolic fistula occurred on an average five years after the initial gastroenterostomy, but in 1 case twenty-nine years had passed before symptoms of fistula developed, and in another case barely a year had passed before a well developed gastrojejunocolic fistula was demonstrated. The youngest patient to have a fistula was 27 years of age. He had been aware of the presence of a duodenal ulcer since the age of 15 and had had symptoms of gastrocolic fistula for four months prior to registration at the clinic. Gastroenterostomy had been performed when he was 18 years of age, and he had had two subsequent operations for ulcer at the anastomosis. The oldest patient was 65 years of age when repair of the fistula was attempted. The average age of the patients was about 46 years.

SYMPTOMS

The symptoms heralding the development of gastrojejunocolic fistula usually are easily distinguished. The history and the aspect of the patient are rather typical. The story is one of long-standing recurrent distress from the ulcer, for which gastroenterostomy first had been performed and occasionally had been followed by other operative attempts to control the continued distress caused by the anastomotic ulcer. A gastrojejunocolic fistula cannot develop unless the anastomotic ulcer is present first. The severe pain of anastomotic ulcer and a shift of pain from the epigastrium to the umbilical region and left side of the epigastrium occur. In the absence of a definite fistula, symptoms of colonic irritation are suggestive of an impending break into the colon. A roentgen diagnosis of gastrojejunal ulcer prior to establishment of a communication between the stomach and the colon was made in a large percentage of cases in this series. In about 30 per cent of the cases the patient had had hemorrhages of various degrees of severity from the anastomotic ulcer before development of the fistula.

With establishment of the fistula the pain usually ceases and diarrhea begins. The stools are usually watery and copious and finally contain large quantities of undigested food which has recently been ingested. Occasionally the patient has a ravenous appetite, but usually there is anorexia with marked loss of weight. Hemorrhage occurred after development of the fistula in 10 per cent of our cases; in 30 per cent of these it occurred before final establishment of the fistula. Frequently patients with gastrojejunocolic fistula complain of a bad taste in the mouth, and about 60 per cent of them will notice foul-smelling eructation. One patient belched while lighting a cigaret and was amazed to see a flare of flame. Fecal vomiting, which usually occurs late in the course of the disease, is found in 15 per cent of the cases. Dehydration, emaciation and nutritional edema may develop rapidly, depending on the size of the opening and the quality of the diet. If the symptoms are allowed to progress unchecked by reparative procedures, pellagra may develop. In a large percentage of cases avitaminotic manifestations of lesser degree will develop.

On admission to the hospital for preoperative preparation, only 13 of the 49 patients were in good condition; 8 more were in relatively good condition. Twenty-seven had edema of the limbs, the abdomen or the face in varying degrees; marked emaciation and loss of weight were the rule. Twenty patients showed some evidence of avitaminosis, and 9 had associated mental derangement, dermatitis and glossitis. One patient had definite carpopedal spasm. Serious anemia was present in only a few cases; in these cases hemorrhage had occurred.

DIAGNOSIS

The diagnosis of a well developed gastrojejunocolic fistula when the history and the aspect of the patient are kept in mind is not difficult. In about a fourth of the cases an inflammatory mass can be palpated in the epigastrium or just above the umbilicus. If roentgen studies are to be made, the method of choice includes a barium sulfate enema. In these 49 cases a well developed fistula was present, yet a positive roentgen diagnosis was made in only 13 of the 40 cases in which roentgenograms of the stomach were made. In 25 cases in this series roentgen examination of the colon was made after a barium sulfate enema had been given; the fistula was demonstrated in each instance.

The laboratory studies with the exception of the chemical findings of the blood and the values for serum protein were not remarkable. A slight hypochromic anemia was usually present. In cases in which repeated hemorrhage had occurred, rather serious anemia prevailed. The gastric acidity was slightly elevated in those cases in which intervening partial gastric resection had not been performed for gastrojejunal ulcer, but the total acidity was never more than 100 or the free hydrochloric acid ever more than 65 (Töpfer's method). The usual test meal

revealed a total acidity of about 50 and free hydrochloric acid of 35 to 40. In the cases in which gastric resection had been performed, the total acidity and free hydrochloric acid were markedly lowered. The total protein was determined in 17 cases; in 11 the value was less than 5 Gm. per hundred cubic centimeters of serum at the time of admission. The albumin-globulin ratio was disturbed to some extent in most of the cases. The level of vitamin C in the plasma was not determined in enough cases to warrant definite conclusions. However, the test was carried out in 7 cases. Normal values range from 0.9 to 1.5 mg. per hundred cubic centimeters of plasma; in only 1 of the 7 cases did the level of vitamin C fall within normal limits. In the remainder it varied from 0.49 to 0.8 mg. per hundred cubic centimeters.

PREOPERATIVE PREPARATION AND ITS EFFECT ON OPERATIVE MORTALITY

Preparing these patients thoroughly and adequately for the extensive operative procedures necessary to effect a cure presents a formidable problem. As can be seen, the clinician is dealing with a patient who is surviving with difficulty the ravages of inanition and whose reserve for reparative processes after operation is low. Furthermore, the chemical constituents of his blood are out of balance, and his courage and will to live are at low ebb because of the nature of his disease. The surgeon cannot assume the responsibility of an attempt at closure of the fistula until the patient has regained some measure of strength and reserve, and the grave risk attending surgical procedures on such patients is obvious.

In this series of 49 cases there were 18 postoperative deaths, a mortality rate of 36.7 per cent. As already pointed out, cases in which the surgeon noted an impending fistula and in which the mortality rate was greatly lower were not included. In order to determine to some degree the effect of preoperative preparation of the patients on the operative mortality rate, they were divided into three groups.

Group 1.—This group consisted of 13 patients (26.5 per cent of the series) who seemed in good condition on admission to the hospital. Seven were considered such good risks that operation was performed on them the day after admission. The chemical constituents of the blood, the serum protein and the results of routine blood studies were normal in 11 cases. None of the patients in this group showed clinical evidence of avitaminosis, but 5 had edema of either the ankles or the abdomen. Because of these findings, the hazards of the proposed operation were thought to be greatly less and meticulous preoperative preparation was thought unnecessary. Yet this group of patients in relatively good condition ultimately did far worse after operation than

another group who were so ill on admission that careful preparation was necessary before they could be subjected to operation.

The average stay in the hospital before operation was less than two and a half days. In no case was an attempt made to cleanse the colon with repeated enemas, to give vaccine intra-abdominally or to administer low residue or residue-free diets. Three of the patients were given fluids by the intravenous route before operation, usually a 5 per cent solution of dextrose in distilled water. No attempt was made to increase the body's store of vitamins. Eight of 13 patients died after operation (a mortality rate of 61.5 per cent). Nearly half (44.4 per cent) of the deaths in the entire series occurred in this small group.

Because of the high operative mortality rate in this small group of cases in which preoperative preparation was not given, it was interesting to study the effect of preoperative preparation on the mortality rate. This study was undertaken with groups 2 and 3 to determine if possible what method of preparation would give the patient the best chance of cure.

Group 2.—This group consisted of the remaining 36 patients, who were considered more thoroughly prepared for operation. Ten died (a mortality rate of 27.7 per cent). A little more than half (55.6 per cent) of the deaths in the entire series were in this group, yet the mortality rate (27.7 per cent) was definitely lower than that of the whole series (36.7 per cent).

The average preoperative stay in the hospital was seven and seven-tenths days. When chemical examination of the blood revealed abnormality, the patient was kept long enough to permit the amount of urea and chlorides and the carbon dioxide–combining power of the blood to return to normal. In the majority of cases vitamins, usually two capsules of halibut liver oil and six tablets of brewers' yeast daily, were given routinely. In 19 cases cleansing enemas were given night and morning for two or three days before operation, and low residue or residue-free diets were employed throughout the preoperative period. In 15 of the 19 cases, 0.5 to 1.0 cc. of vaccine was given intraperitoneally in addition to the regular preparation of the colon. The prothrombin time (Quick test) was normal in instances in which it was obtained. Vitamin K was not given to the patients in this group. Fluids, usually a 5 per cent solution of dextrose in a 0.9 per cent solution of sodium chloride, were given intravenously to 24 of these 36 patients.

Group 3.—This group consisted of 7 patients who also were included in group 2. These patients are grouped separately because their preoperative preparation was as thorough as possible, and only 1 postoperative death occurred. All 7 of these patients were in worse condition on admission than the average patient of the total series. All were greatly emaciated, and 6 had marked nutritional edema of the ankles

and the abdomen. One had rather serious pyelonephritis, and another had mild mental changes, which together with his avitaminotic state and dermatitis suggested pellagra. The chemical findings in the blood were not more abnormal than is usual in this type of case, but in 2 cases the values for the proteins were less than 5 Gm. per hundred cubic centimeters of serum. Determinations of vitamin C in the plasm were made in only 3 of these cases; the values were below normal in all 3. However, in these 7 cases there was only 1 death, and that occurred on the seventeenth day after operation and was caused by peritonitis. Perhaps the fact that each of the patients was in even worse than usual condition on admission led to more painstaking preparation for operation. A postoperative mortality rate of only 14.2 per cent after repair of gastrojejunocolic fistula performed in one stage in 7 such cases is remarkable.

The average preoperative stay in the hospital for these 7 patients was slightly more than nine days. They all received daily at least 2,000 cc. of a 5 per cent solution of dextrose in a 0.9 per cent solution of sodium chloride intravenously. Two received transfusions of 500 cc. of citrated blood. In each case the colon was prepared in the usual way; that is, cleansing enemas were given morning and night for two or three days before operation. In addition, all patients received vaccine intraperitoneally, low residue diets and massive doses of added preparations of vitamins daily, the exact amounts depending on the patient's needs. The usual routine for the daily administration of such vitamins included: (1) 100 to 200 mg. of ascorbic acid orally or 100 mg. intravenously; (2) 100 to 150 mg. of nicotinic acid orally or 50 to 100 mg. intravenously; (3) 15 to 30 mg. of thiamine hydrochloride orally or 5 to 15 mg. intravenously; (4) 30 drops of percomorph liver oil; (5) some form of vitamin D (halibut or cod liver oil in bulk or capsules); (6) six to twelve tablets of brewers' yeast daily. These amounts were varied according to the patient's needs.

From study of groups 2 and 3 it is clear that no single therapeutic measure will cause significant lowering of the operative mortality rate. Each patient must be studied and treated individually. Hard and fast rules of preoperative management cannot be given, although a logical rationale of preoperative management is suggested by this study.

SURGICAL CONSIDERATIONS

If a procedure of one stage is contemplated for the repair of a gastrojejunocolic fistula, some such method of preoperative management would seem wise. Preliminary jejunostomy is recommended by some surgeons and in their experience has given good results. Scrimger [8]

8. Scrimger, F. A. C.: A Technic for the Management of Gastrojejunal Ulcers With or Without Gastrocolic or Jejunocolic Fistula, Ann. Surg. **104**:594-600 (Oct.) 1936.

suggested a technic in which the edges of the gastric mucosa from the cuff of the anastomotic ulcer are sutured together over the fistula; a posterior Polya type of gastric resection is then carried out, utilizing portions of the jejunum distal to the fistula. In 5 cases reported, 1 death occurred. One patient in our series was subjected to preliminary jejunostomy but died thirteen days after the operation of perforation of a gastric ulcer and resulting peritonitis and uremia. Many other suggestions of technic have been advanced, occasioned no doubt by the high mortality rate attending the accepted types of repair. Allen [8] has suggested resection of the colon, jejunum and stomach en masse by the Kerr aseptic technic of anastomosis for restoration of continuity of the gastrointestinal tract. Finsterer [9] preferred to carry out the procedure in a single stage but recommended an operation in two stages if simple closure of the fistula could not be performed. Findlay [10] recommended a multiple stage operation.

Perhaps one of the most encouraging suggestions is that of Pfeiffer,[11] who recommended preliminary loop colostomy in preparation for final repair of the fistula at a second stage. In this way the fecal current is diverted above the fistula, giving the inflammatory process at the site of the fistula time to heal and averting colonic contamination. The general condition of the patient can be improved greatly in this way in preparation for final repair of the fistula.

SUMMARY

A series of 49 cases in which patients were operated on at the Mayo Clinic from 1930 to 1939, inclusive, is reviewed from the standpoint of medical preoperative management. Of the 49 patients, 18 died after operation; the mortality rate was 36.7 per cent. Of 13 patients who received practically no preoperative preparation, 8 died; the mortality rate in this group, then, was 61.5 per cent. Of the remaining 36 patients, all of whom had fairly satisfactory preparation, 10 died—a mortality rate for this group of 27.7 per cent.

Only 1 of 7 patients, all of whom were in worse condition on admission than usual and who received careful and adequate preoperative treatment, died—a mortality rate of 14.2 per cent.

It is suggested the prohibitive mortality rate after reparative procedures performed in one stage for gastrojejunocolic fistula can be lowered materially by adequate preoperative management.

9. Finsterer, H.: Results of Repeated Operations upon the Stomach Especially for Gastrojejunal Ulcers, Surg., Gynec. & Obst. **68**:334-346 (Feb. 15) 1939.

10. Findlay, F. M.: Treatment of Gastrojejunocolic Fistula by Multiple Stage Operations, Arch. Surg. **32**:896-906 (May) 1936.

11. Pfeiffer, D. B., and Kent, E. M.: The Value of Preliminary Colostomy in the Correction of Gastrojejunocolic Fistula, Ann. Surg. **110**:659-668 (Oct.) 1939.

CONGENITAL DUODENAL OBSTRUCTION

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Acute intestinal obstruction is always such a serious illness that it demands prompt recognition and treatment to prevent a fatal termination. This is just as true when it occurs in infants as when it occurs in adults, with the further consideration that infants, being inarticulate, often are subjected to delay in diagnosis, and this results in their contributing more than their share to the high mortality rate.

When one is reminded that the first successful operation for the cure of duodenal obstruction in an infant was reported as recently as 1916,[1] there seems some justification for the past failures of those responsible for the medical care of infants to recognize the condition. That the point in pediatrics has been reached where the disease, whether acquired or congenital, is more promptly recognized is attested by the increasing number of cases reported. There has been an unjustifiable tendency to consider gastric and intestinal disorders of the baby as errors of digestion or nutrition, but this diagnostic complacency is rapidly being displaced by scientific and common sense observation on the part of physicians.

Congenital duodenal obstruction is not a common condition, but its frightful mortality rate gives it an importance among the diseases of infancy and childhood second to no other illness.

A brief résumé of the mechanical factors involved is a good background for the consideration of the symptoms and treatment. In the second and third month of fetal life,[2] the entire gastrointestinal tract is a simple rod of epithelium and mesoderm, with practically no lumen. The cephalic end dilates into a rudimentary stomach, the midportion

1. Ernst, N. P.: A Case of Congenital Atresia of the Duodenum Treated Successfully by Operation, Brit. M. J. **1**:644 (May 6) 1916.

2. Callander, C. L.: Surgical Anatomy, Philadelphia, W. B. Saunders Company, 1933. Arey, L. B.: Developmental Anatomy, ed. 3, ibid., 1934.

grows in length and assumes the form of superimposed coils, while the caudal extremity dilates slightly to become eventually the sigmoid flexure and the rectum. All of this embryonic tract lies on the left side of a shallow abdomen. The small bowel increases in length and projects itself, for lack of space, into and through the umbilicus into the cord so that, in reality, a hernia is created. For some reason unknown to those best qualified to state, the small bowel is retracted soon after and

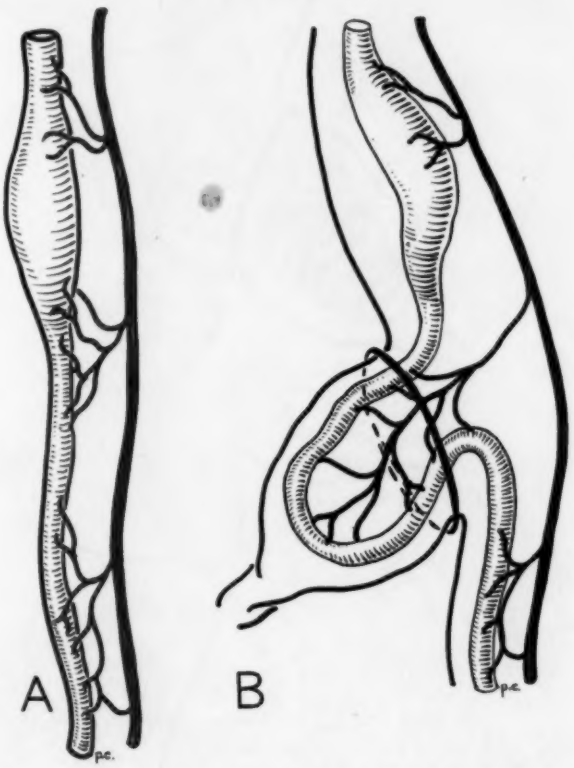

Fig. 1.—*A*, primitive gastrointestinal tract. *B*, elongation of the small intestine and its projection through the umbilical canal.

returns to the left side of the abdomen. An unyielding short mesentery is one explanation of the out and in mechanism. In the upper left quadrant of the abdomen, in the region of the spleen the large bowel joins with the small intestine and extends directly downward to become later the descending colon, sigmoid flexure and rectum. About the third month, the colon grows in length, pushing the cecum, which has been in the region of the spleen, over into the lower right quadrant of the abdomen, where it becomes firmly attached. This is known as the rota-

tion of the colon. In this movement, the leaf of the mesentery and the superior mesenteric artery are involved and apparently angulated to some extent. The colon continues to grow two of its fixed points, the

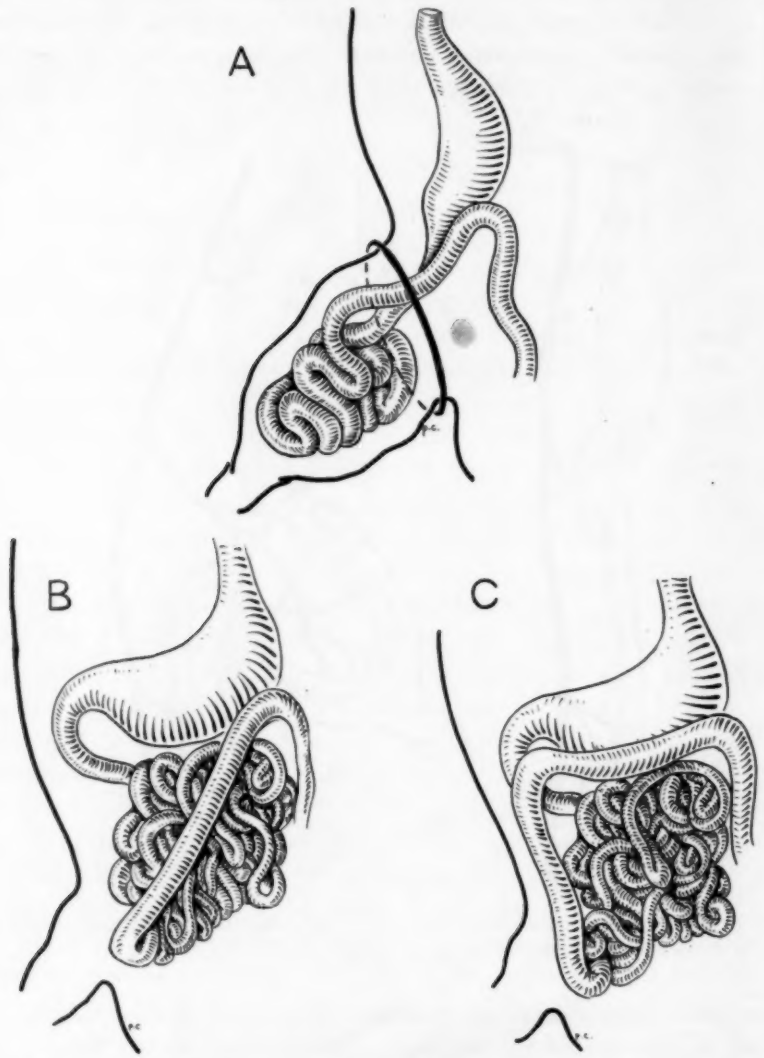

Fig. 2.—*A*, the small intestine greatly increases its length. *B*, the colon descends and rotates. *C*, the colon elongates to form the ascending and transverse colon.

lower right and the upper left quadrant of the abdomen, and the additional length goes into the space formerly occupied by the liver. The liver, which has been a relatively large organ up to this time, either

recedes beneath the ribs or actually diminishes in size. The portion of the large bowel filling this space becomes the ascending colon, hepatic flexure and transverse colon and covers the duodenum and proximal part of the jejunum. It is in this development and rotation that deviation from the normal manner results in angulation or compression of the duodenum. In all but 1 of every 20,000 cases the adjustment is perfect

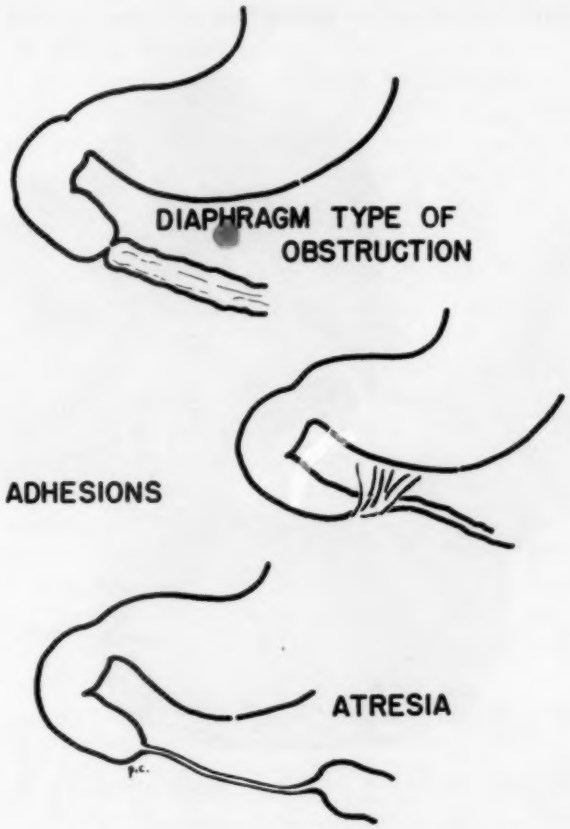

Fig. 3.—The types of duodenal obstruction.

and the function of the intestine is uninterrupted. The 1 case is that of duodenal obstruction.

Other forms of obstruction are recognized anatomically. An unusual type is one in which a diaphragm or septum develops within the duodenum; this is known as an intrinsic obstruction. The most common obstruction is the atresia or failure of the bowel to develop a lumen, leaving the intestine merely a stringlike continuation of the duodenum. This may be and often is multiple. It seems futile to seek an explana-

tion for these errors and defects in development; it is sufficient today to recognize their presence.

In most cases, the obstruction dates from birth, and, except in those rare ones in which an incomplete diaphragm is present in the duodenum, the onset of symptoms is prompt and continuous. Vomiting stands out as the most conspicuous and important symptom and is therefore entitled to the most careful consideration. It appears shortly after birth and continues until it is relieved by appropriate measures or until the patient

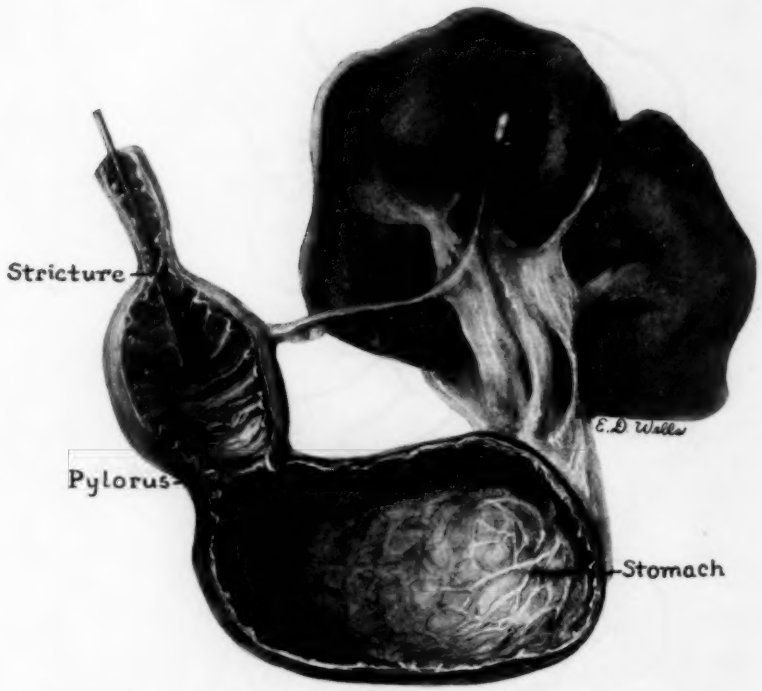

Fig. 4.—Specimen showing the intrinsic or diaphragmatic type of obstruction.

succumbs. It does not follow feeding as promptly as in pyloric stenosis, and in most instances bile and duodenal contents (readily recognizable by odor and color) are present.

The stomach may be dilated, and the physical examination should demonstrate this; the lower part of the abdomen, however, will be flat. There should be no hesitation in using a thin feeding of barium sulfate to outline the stomach and duodenum and thus localize the obstruction. As a rule, the stools consist chiefly of meconium.

It has been pointed out that if the lesion in the duodenum is proximal to the opening of the common bile duct, bile will not appear in the

vomitus, and a picture identical with pyloric stenosis presents itself. A diagnosis of this condition in itself is no great commission of error if the obstruction is recognized and treated surgically when the differentiation is made at the time of operation. Suffice it to state that other symptoms of intestinal obstruction are present, and the recognition of the condition should not be insurmountable. Too much emphasis cannot be placed on the necessity of furnishing food and fluid to the dehydrated and starved victims of obstruction prior and subsequent to surgical measures.

In a reasonable search of the literature, we have found no accurate study made of comparative blood counts and blood analyses in these cases, but we have no doubt that they run parallel to those in the cases of adults. In the latter, moderate leukocytosis, decrease in chlorides and hypoproteinemia are the major changes. This should prove a valuable and interesting study.

It would seem that the urgency of these cases demands prompt diagnosis and surgical treatment. If there is any medical situation in which time is an element in the treatment, it must be acute intestinal obstruction in infants. In too many cases operation is postponed until no hope of a successful outcome can be entertained.

The diagnosis in most cases can be made on the basis of the short period after birth in which vomiting occurs, together with the persistence and type of the vomiting and the nature of the material ejected. Roentgen examination is of positive value and should be utilized more frequently. If the physician expects to delay and fortify the patient by intravenous injection of solutions or of blood, he is doomed to disappointment. The catalytic elements in the disease outweigh the constructive assistance furnished by parenterally injected solutions. McIntosh and Donovan [3] observed:

> Some of the authors writing on this subject have laid emphasis on the part played by volvulus in producing the symptoms of obstruction, while others have stressed the kinking and compression of the duodenum by congenital peritoneal bands and the constricting effect of other malformations of the mesentery. Our series includes examples of all of these types, and we wish to point out that preoperative differentiation among them is always difficult and often impossible.

The treatment is surgical. The intravenous injection of solutions prior to the operation is recommended, but temporizing with the hope of raising the resistance of the patient is not justified in the light of experience. Plasma is the logical substitute for blood and should be used freely.

There is no necessity for detailing the steps of the operation. The operator should always bear in mind that the patient offers a poor

3. McIntosh, R. R., and Donovan, E. J.: Disturbances of Rotation of the Intestinal Tract, Am. J. Dis. Child. **57**:116-166 (Jan.) 1939.

risk, that no time must be wasted, that one of several operations is permissible and that the tissues involved are often of transparent thinness and permit only the gentlest manipulation. With these facts before him, he should see to it that the stomach has been lavaged, that the child is well protected by warm coverings, that the induction of anesthesia is in capable hands and that the after-care, particularly the feeding, is supervised by one of wide experience. The absence of any one of the foregoing essentials may lead to an unnecessary fatality.

The types of operations in general use are as follows: liberating adhesions, opening the bowel, dividing the diaphragm and closing the opening in the bowel, gastroenterostomy, duodenojejunostomy. Ladd, who has had wide experience and has reported more personal cases than any one else, prefers an operation that bears his name for the extrinsic obstructions. All types of operations are difficult and attended with considerable mortality. It will require further study of the patients who have recovered, after the lapse of several years, as well as of those who have succumbed, to propose a basis for a standardized operation for each type of obstruction. No type of enterostomy has been successful, and this procedure should be eliminated as a palliative or curative measure.

Up to 1932, Ladd could find but 10 cases in which there had been successful operation, and of these he had 7. To illustrate the celerity with which the disease has been recognized, in 1937 Ladd [4] reported 28 additional cases in the Childrens' Hospital in Boston. His great experience gives weight to his statements, and we quote almost verbatim from a description of his operation. The procedure consists of a long incision of the right rectus muscle through which the entire small intestine is delivered and unrotated if a volvulus is present. In one or two instances this gave relief at once but later proved insufficient. The next step consists in mobilizing the ascending cecum and the proximal half of the transverse colon until the duodenum is completely visible. If there are any folds of peritoneum or bands which impinge on the duodenum and constrict it, they are severed, care being taken to protect the superior mesenteric artery. Ladd had 19 recoveries in 23 cases, with a satisfactory follow-up record.

We have operated on 4 such patients. The first we lost by failure to recognize the nature of the obstruction, which was of the intrinsic type. The remaining 3 had obstruction of the extrinsic or adhesion type and were treated by gastroenterostomy. We probably did not employ the best type of operation, but in 2 of the cases we felt that the condition was so critical that evisceration and mobilizing the colon would

4. Ladd, W. E.: Congenital Duodenal Obstruction, Surgery **1**:878-885 (June) 1937.

have been more than the patient could survive. The 3 patients have gained weight and thrived. They will furnish subjects for an absorbing study in years to come. We are of the opinion that Ladd's operation is rational and the one of choice, but in exceptional circumstances another operation meets the situation quite as well.

SUMMARY

Congenital duodenal obstruction is an uncommon condition and highly fatal in the absence of prompt diagnosis and treatment. Vomiting is an early and persistent symptom and should arouse suspicion of intestinal obstruction in the newborn. Bile is usually present in the vomitus. While the exact nature and location of the obstruction cannot always be known before operation, a diagnosis of intestinal obstruction is possible early in the majority of cases. The taking of a "scout" roentgen film or of a film after the oral administration of barium sulfate is both safe and desirable. Operation is the only treatment which offers a hope of cure but must be employed early, preferably by one with experience in pediatric surgery.

Dehydration and shock should be combated by parenteral administration of fluids, of which plasma is the most valuable.

The preoperative and the postoperative care rank equally high in importance with the operation. Our preference is for general anesthesia induced by administration of ether by the drop method. Many prefer local anesthesia. All types of anesthetization demand the services of a competent anesthetist.

PROGRESS IN ORTHOPEDIC SURGERY FOR 1940

A REVIEW PREPARED BY AN EDITORIAL BOARD OF THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS

(*Continued from page 734*)

XIV. CONDITIONS INVOLVING HIP JOINT

Anatomy and Physiology.—The use of multiple drill holes to revascularize the head of the femur has now become common. Compere, Garrison and Fahey [428] have investigated experimentally the possibility of permanent injury to the capital and greater trochanteric epiphyses by multiple drilling. One or both of the two major growth centers of the proximal end of one femur in each of 27 goats 6 weeks old were subjected to operative trauma by curettage or multiple drilling. After maturity had been reached, nineteen months later, the animals were killed, necropsy was performed, and the femurs were removed for study, measurement and roentgen examination. The authors conclude that surgical trauma to the greater trochanteric epiphyses by drilling or curettage causes arrest of growth with resulting deformity and shortening of the greater trochanter and associated coxa vara. Similar surgical trauma to the epiphysial cartilage plate of the head of the femur usually results in arrest of growth, which produces a shortening of the neck of the femur, an irregular contour of the head of the femur, coxa vara and a functional shortening of the shaft of the femur. The authors conclude from their experimental work that drilling the neck of the femur of a young child to hasten revascularization of the head, as in cases of Legg-Perthes disease, is a questionable procedure.

Mouriquand, Dauvergne and Edel [429] report further results of prolonged experimental deficiency of vitamin C in dogs. They have been able to demonstrate that deficiency of vitamin C of sufficient duration produces decalcification of the bones, mostly at the extremities, calcium deposits and formation of new bone in the subperiosteal regions and in the soft tissues in the neighborhood of joints. They have found that the effect in the head of the femur is so pronounced that it becomes

428. Compere, E. L.; Garrison, M., and Fahey, J. J.: Deformities of Femur Resulting from Arrestment of Growth of Capital and Greater Trochanteric Ephipyses, J. Bone & Joint Surg. **22**:909-915 (Oct.) 1940.

429. Mouriquand, G.; Dauvergne, M., and Edel, V.: Irreversible Decalcification of Femoral Neck in Chronic Vitamin C Deficiency, Presse méd. **48**:268-269 (March 12) 1940.

completely decalcified. While the outline of the head and the neck of the femur disappears, the acetabular cavity becomes filled with bony proliferations. Similar results, although less marked, are produced by a diet only partially deficient in vitamin C (e. g. one containing 0.5 mg. of ascorbic acid per day). This curious syndrome, once produced, is irreversible, and recalcification of the head and neck of the femur could not be effected either by supplementing the diet with as much as 50 mg. of ascorbic acid per day for as long as one hundred and eleven consecutive days or by the administration of massive doses of vitamin D. The authors suggest that the physician bear their experimental findings in mind when confronted with decalcification of obscure origin localized in the head and the neck of the femur of a child.

Bifurcation Operation on the Hip.—Milch [430] advocates the bifurcation operation because it is a simple procedure which can be quickly performed and which gives a stable hip and relieves pain. The objection to this operation is that it produces knock knee and limitation of motion. Milch feels that the knock knee deformity is not of great significance.

He has observed a tendency in children for the original bifurcation to disappear and for the spike of bone which constitutes the upper end of the distal fragment to be absorbed. In adults this change in the configuration of the bone does not take place. Disability occurs in cases in which the anomaly is unilateral; it becomes well pronounced in many cases in which the bifurcation operation is performed on both sides. This disability is associated with limitation of abduction, rotations and flexion. The patient has a distinct waddle in walking because he cannot bring his legs together in the normal fashion. Milch notes in children that as the spike disappears these symptoms are gradually improved. He argues that this is an indication for the removal of the spike. In adults with pronounced symptoms there were marked increase in the range of motion of the joint and absence of pain after the spike was removed. He believes that the spike is not essential to successful osteotomy but that on the contrary it is the cause of the undesirable effects found almost routinely after a typical bifurcation operation.

Slipped Epiphyses.—Ghormley and Fairchild [431] in a general discussion of slipped epiphysis of the femur emphasize that the term "slipped epiphysis" is a misnomer, because the epiphysis retains its position in the acetabulum while the neck and shaft of the femur rotate externally and ride upward. They point out that Milch proposed the term "epiphysial coxa anteverta" and that the term "epiphysiolysis" is apt but will probably not supersede the commoner expression "slipped epiphysis."

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430. Milch, H.: Bifurcation Operation, Surgery **8**:686-698 (Oct.) 1940.

431. Ghormley, R. K., and Fairchild, R. D.: Diagnosis and Treatment of Slipped Epiphyses, J. A. M. A. **114**:229-235 (Jan. 20) 1940.

Pitzen [432] distinguishes three types of coxa vara: the congenital, the rachitic and the adolescent or static. Congenital coxa vara is due in his opinion to a disturbance of endochondral ossification, which is shown in roentgenograms as a rarefaction in or lateral to the epiphysial line. [ED. NOTE: However, he presents no evidence for this opinion.] Coxa vara in adolescent patients he ascribes to a softening process in the metaphysis of the neck of the femur which allows the epiphysis to slip downward and backward, a shift demonstrable in a lateral roentgenogram. He describes the histologic characteristics of osteomalacia localized in the metaphysis of the neck which he concludes is associated with disturbance of the internal secretions of the gonads and the hypophysis. [ED. NOTE: No detailed evidence for these conclusions is presented, and the histologic observations, if corroborated, are open to another interpretation, namely, that the rarefaction is secondary to the slipping.]

Waldenström [433] also feels that the condition is fundamentally due to an endocrine disturbance of the adiposogenital type. He believes that this disturbance may be transitory. Waldenström judges the length of time during which slipping may occur by determining the maximum time between the onsets of slipping on one side and the other when the anomaly is bilateral. In his series of cases the interval has been one and one-half years. However, it is becoming increasingly apparent from the literature that by no means all, in fact only the minority, of the cases are of the so-called endocrine type. This is brought out by Ghormley and Fairchild, who, after reviewing the trauma, infection and endocrine disturbance hypotheses of causation, conclude that trauma together with the mechanical disadvantage of the epiphysial plate is probably the usual, if not the sole, cause of displacement. The mechanical disadvantage is greater during adolescence because of the relatively increased weight of the body and the obliquity of the epiphysial line. With this in mind they discuss the types of patients and show that in their series 18 patients were normal in weight and 26 were obese or of unusually large build. However, of the latter 26, 14 were constitutionally obese and for only 12 was there sufficient evidence to suggest some endocrine syndrome.

To test Brailsford's [434] hypothesis that slipping of the epiphysis is due to renal rickets, Waldenström carefully examined 7 consecutive patients by clinical and laboratory means for evidence of renal rickets.

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432. Pitzen, P.: Coxa Vara: Its Causes and Treatment, Med. Klin. **36**:344-347 (March 29) 1940.

433. Waldenström, H.: Slipping of Upper Femoral Epiphysis, Surg., Gynec. & Obst. **71**:198-210 (Aug.) 1940.

434. Brailsford, J. F.: The Radiology of Bones and Joints, ed. 2, Baltimore, William Wood & Company, 1935.

Finding none, the author concludes that renal rickets is at most a rare cause of epiphysiolysis.

All these authors point out that any adolescent patient complaining of slight pain or limp should be regarded as possibly having a slipped epiphysis. The importance of a careful examination of an adolescent patient complaining of pain in the hip is emphasized. They show that the early signs of slipped epiphysis may be minimal and that there is only a slight limitation of internal rotation as compared with the rotation on the normal side. Roentgen examination should therefore include the sound side. Anteroposterior and lateral views are of equal importance.

Waldenström insists that roentgenograms should always be taken simultaneously, in the same relative position and at the same distance. The lateral view is taken with the hips flexed and abducted. This view he finds most helpful, and he says it should never be neglected. The significant roentgenographic appearances are three: The epiphysial hook is down; the metaphysial edge is up, and there is a broader epiphysial line.

Ghormley and Fairchild indicate the general dissatisfaction with the results of treatment. They state that all authors agree that the various stages of the condition require different methods of treatment and that few advocate one method to the exclusion of others.

They divide their treatment of the various stages as follows:

1. In the early slipping stage conservative treatment is advocated with discontinuance of weight bearing by crutches or a walking caliper splint until union of the epiphysis occurs.

2. (*a*) In the stage of gradual slipping the epiphysis is not completely separated and cannot be reduced by manipulation without injury; open operation with osteotomy of the neck of the femur is advocated as the treatment of choice.

(*b*) In the stage of acute slipping superimposed on a gradual slipping or a preslipping stage a manipulative closed reduction is recommended if it is certain that the epiphysis is completely loose; if doubt exists, open reduction should be done.

3. In the stage of complete slipping of long standing treatment by open reduction or cervical osteotomy is recommended if the epiphysis is fused. They believe adults are best treated by arthrodesis if pain is pronounced or by acetabuloplasty if motion is to be preserved.

Pitzen considers nonoperative and operative methods. The former consist of traction, of freedom from weight bearing enforced by use of a plaster cast or an apparatus and maintained until fusion of the epiphysial line occurs and of reduction by manipulation in cases of recent slipping. Traction is used for young children, patients with rickets and some patients with recent epiphysiolysis. The reduction by manipulation is

followed by immobilization in plaster for some six to eight weeks with the leg in 30 degrees of abduction with full extension and internal rotation. For operative treatment, the author favors oblique osteotomy through the femur at the level of the lesser trochanter. In cases of absorption of the neck of the femur, this procedure may be combined with the use of a triflange nail. Other operative procedures are discussed but not advocated.

Rabinowitz [435] recommends reduction by manipulation with the patient under anesthesia followed by the application of a spica to the hip with the leg in a position of abduction and internal rotation. Weight bearing with crutches is begun at once and continued for twelve weeks; then the spica is removed, and crutches are used for a further period of five or six weeks. The author claims that this method offers many advantages because of its simplicity, economy and effectiveness and because it permits a wider range of activity and a better mental attitude to the patient. It is notable, however, that in 6 of the 8 cases reported the anomaly was in the early or preslipping stage.

Waldenström states that adhesive or skeletal traction with the leg in abduction gives suitable results in the early stage if combined with protected weight bearing for one year but that it does not always prevent recurrence. He condemns manipulation with the patient under anesthesia; reduction is usually not obtained, and in 20 per cent of all cases aseptic necrosis of the head of the femur follows. Reposition by means of arthrotomy may give excellent results, but he finds this method inadvisable since it, too, is attended by the risk of aseptic necrosis. In his opinion the procedure of nailing described by Wilson [436] is the treatment of choice for the early stages as it prevents recurrence, allows early motion, produces premature fusion of the epiphysis and is attended with excellent results. For further advanced stages of marked epiphysiolysis a cuneiform torsion osteotomy is advocated.

In cases in which union has occurred with deformity, King (T.) [437] advises against open reduction because there is sufficient interference with the circulation to lead to aseptic necrosis. He favors subtrochanteric osteotomy of the cuneiform type. Removal of a wedge sufficiently large to produce an angle of 150 degrees between the neck and the shaft of the femur is necessary to restore the normal relation of 130 degrees and to bring the epiphysial line into a nearly horizontal position. The posterior displacement of the head on the neck of the femur is corrected

435. Rabinowitz, M. S.: Slipping of Upper Femoral Epiphysis, J. Bone & Joint Surg. **22**:992-998 (Oct.) 1940.

436. Wilson, P. D.: Conclusions Regarding the Treatment of Slipping of the Upper Femoral Epiphysis, S. Clin. North America **16**:733-752 (June) 1936.

437. King, T.: Value of Femoral Osteotomy for Diseases and Injuries of Hip Joint, M. J. Australia **1**:253-268 (Feb. 24) 1940.

by cutting the wedge with its base facing the anterolateral surface of the shaft of the femur. The operation in cases of this type requires careful planning from a study of the lateral roentgenogram. The author states that postoperative roentgenograms show gradual restoration of the contour and of the relation between the head and the neck of the femur.

[ED. NOTE: It is the view of one of us (L. C. A.) that early stages of minimal displacement should be treated by nailing through a lateral incision. In the more advanced stages open reduction of the displacement should be done if the line of junction can still be seen distinctly in a roentgenogram. Great care is essential in the preservation of the blood supply of the head and the neck of the femur. In the late stages osteotomy is the preferred procedure.]

The 8 cases reported by Rabinowitz include follow-up examinations for nine months to four and one-half years, and the results are given as excellent. In no case did the slipping progress. In all but 1 the involved epiphysis was fused at the end of treatment; in all cases the epiphysis on the opposite side remained unfused. Nicolaysen [438] reports 9 cases in which the treatment consisted of closed reduction and immobilization in a plaster cast in the Whitman position and 9 in which more conservative methods were employed. All but 1 were followed for one and one-half to nine years. The end results were judged on the basis of shortening, muscular atrophy and mobility according to the Ferguson and Howorth index and anatomically from roentgenograms. In 13 cases the results were good to excellent; in 3 good, and in 2 fair. He concludes that the results of closed reduction were in every respect superior to those of more conservative methods.

Ghormley and Fairchild give the results of the treatment of 55 patients seen at the Mayo Clinic from 1922 to 1936. Of these, 43 were male, and 12 were female. In 6 cases the anomaly was bilateral. The average age of the patients was younger for girls than for boys. Manipulation was used in 8 carefully selected cases with good results in 6, fair in 1 and poor in 1. The authors emphasize that manipulation should be gentle and should be employed only in carefully selected cases. In 6 cases, open reduction was carried out; good results were obtained in 2, fair in 1 and poor in 1. A bone screw was employed in 1 case; the result was a complete failure. The outcome in 1 case was unknown. In 11 cases a wedge of bone was removed from the neck of the femur; results were good in 6, fair in 3 and poor in 1; in 1 case removal was too recent to permit the formation of an opinion. Conservative treatment by means of a brace or crutches was used in only 4 cases; results

438. Nicolaysen, N. A.: Epiphysiolysis of Head of Femur and Its Treatment, Nord. med. (Med. rev., Bergen) **6**:733-741 (April 13) 1940.

were good in 2 cases, fair in 1 and poor in 1. Of the patients who were in the preslipping or early slipping stage, regardless of the type of treatment, all but 1 showed a good or fair result. The usual treatment was conservative. In 1 case, however, there was progress to a complete slip.

Blood Supply of the Hip.—An adequate blood supply to the head and neck of the femur is now assuming great significance because of the frequency with which aseptic necrosis is encountered in fractures and other lesions. Pollock [439] has restudied the sources of blood supply by arteriography and divides the vessels as follows: (1) the diaphysial group, which springs from the nutrient artery of the femoral shaft; (2) the periosteal group; (3) epiphysial group, which derives from the circumflex artery; (4) the arterial group of the ligamentum teres femoris. Interference with any one source will result in disturbance of bone metabolism proportionate to the importance of the supply affected. Pollock believes that interruption of all four sources will be followed by necrosis of the entire head of the femur. He examined microscopically sections made from 23 heads of femurs in which there was no vascular supply except that carried by the ligamentum teres femoris or by adhesions. He found considerable areas of new bone formation in 22 of the specimens. In 1 there was no formation of new bone, and in this specimen he was able to demonstrate a complete lack of blood supply.

Coxa Plana.—The articles which have appeared on coxa plana or juvenile osteochondritis of the hip (Calvé-Legg-Perthes disease) show a definite tendency toward agreement with regard to treatment and prognosis. The etiology and roentgen pathology are still subjects on which various authors disagree.

Piergrossi [440] and Lehmann [441] state that coxa plana is probably due to primary aseptic necrosis of the head of the femur with similar foci occurring simultaneously in the neck and in the acetabulum and that all the lesions are due to a common cause. Gill,[442] on the other hand, feels that the original site of necrosis is in the metaphysis. "The degenerative changes which occur in the head are also of the nature of aseptic necrosis, and are due to cutting off the blood supply through the metaphysis and the epiphyseal plate." [ED. NOTE: Vessels traversing the epiphysial

439. Pollock, G. A.: Changes Associated with Interference with Blood Supply of Head of Femur, Mil. Surgeon **86**:254-255 (March) 1940.

440. Piergrossi, A.: Lesions of the Femoral Neck in Infantile Osteochondritis of Hip, Radiol. med. **27**:81-108 (Feb.) 1940.

441. Lehmann, J. C.: The Progress of Epiphyseal Necrosis in Roentgenograms, with a Contribution to the Early Diagnosis of Perthe's Disease, Deutsche Ztschr. f. Chir. **253**:132-144, 1940.

442. Gill, A. B.: Legg-Perthes Disease of Hip: Its Early Roentgenographic Manifestations and Its Cyclical Course, J. Bone & Joint Surg. **22**:1013-1047 (Oct.) 1940.

plate have never been described.] This view is supported by Gill's observation that an area of rarefaction may be seen in the metaphysis preceding an epiphysial focus which later appears directly overlying it. Piergrossi points out that the metaphysial lesions may exist without concomitant changes in the epiphysis, leading to infantile coxa vara as described by Bertolotti.

Pathologic data are scarce. Pike [443] studied a specimen removed at autopsy from the body of a 5 year old boy who died of a diaphragmatic hernia after an automobile accident. Although the child had complained of no symptoms referable to the hip, a roentgen examination of the pelvis shortly after the accident revealed flattening and segmentation of the epiphysis, broadening of the neck of the femur and thickening and widening of the joint space. At the time of death, seventy-two days later, the head and the neck of the femur were removed for study. Grossly, fragmentation of the epiphysis with areas of necrosis as well as zones suggestive of a degenerative change in the metaphysis was noted. One section was examined microscopically; this showed

> considerable necrosis proximal to the epiphyseal line with considerable debris. No inflammatory reaction, however, is evident. There is some increased fibrosis and some round cell infiltration near the epiphyseal cartilage. The cartilage shows no actual change. Distal to the epiphyseal line, there is a partial necrosis of bone. The picture is of degeneration without particular inflammatory infiltration. There are areas of apparently dead bone. The marrow spaces are devoid of blood cells. Other areas show fairly normal cellular bone development with regard to cellular nuclei.

Pike states that these changes correspond to those seen by previous authors; he plans further study of the specimen.

Gill emphasizes the importance of early diagnosis and states that the disappearance of slight pain, muscle spasm and limitation of motion after a few days' rest in bed is deceiving. He also states that a firm slight thickening of the hip can almost always be felt by careful palpation.

Two aids in early roentgen diagnosis are described. Lehmann states that if immediate immobilization is carried out once the diagnosis is suspected, the atrophy of disuse in the pelvis and the femurs which ensues will not involve the aseptically necrotic epiphysis, which will present a striking contrast during the succeeding months. Gill finds that slight overexposure of the roentgenograms increases the facility with which the small metaphysial foci may be visualized.

The well known sequence of onset, degeneration and regeneration are described by Pike, Piergrossi and Gill. Piergrossi finds that cystic formations, zones of osseous condensation and shortening and thickening of the neck are the result of the metaphysial lesions and of the

443. Pike, M. M.: Legg-Perthes Disease with Particular Regard to Treatment, Connecticut M. J. **4**:5-11 (Jan.) 1940.

concurrent changes in the periosteum of the neck and in the epiphysial cartilage. These authors agree that the major deformities consisting of flattening of the head of the femur, bowing of the neck and deformation of the acetabulum are the direct result of weight-bearing stresses during the course of the disease and emphasize the necessity for continuous freedom from weight bearing from first suspicion of the disease until the process is completed. This usually requires from two to three years. Pike points out that apparatus is necessary because children in the age group affected by the disease do not lie quietly in bed unless they are forcibly constrained. He advises the use of Buck's extension until pain and muscle spasm are alleviated and then the application of the Wu double hip splint. Other authors use continuous traction extension or immobilization in a plaster of paris cast. Walking calipers and other ambulatory braces are condemned because they allow minor degrees of weight bearing, which may be detrimental.

Ghormley and Fairchild emphasize the need for adequate treatment of osteochondritis and other conditions involving the hip in children because 22 per cent of a series of 154 adult patients seen at the Mayo Clinic had osteoarthritis as a late sequela of a disorder of the hip in childhood.

Gill presents 12 cases, and Pike reports 10, with serial roentgenograms for most of them. Excellent results, evidenced both by clinical and by roentgen examinations, have been obtained by early treatment of the disease in cases in which there was little original deformity of the head of the femur. The patients were restrained from all weight bearing. The normal contour of the head of the femur and the acetabulum was almost completely restored. In cases in which the disease has reached a later stage with marked deformity and fragmentation, but in which it is still in the phase of degeneration, remarkable reformation of the contour of the hip has been achieved by a similar regimen. Lehmann illustrates the result obtained by early and continuous treatment by a series of roentgenograms of a patient with bilateral Legg-Perthes disease. The patient was seen late in the course of the disease in one hip. Healing eventually occurred with marked flattening of the epiphyses. At this time symptoms appeared in the opposite hip, and immobilization in a plaster of paris cast was begun at once. Healing occurred with complete regeneration without deformity.

Ischiopubic Osteochondrosis.—Inclán [444] reports 3 cases of ischiopubic osteochondrosis. It is characterized by pain, limp and limitation of motion of the hip joint, usually after trauma. Differential diagnosis may be difficult. Carefully focused roentgenograms show rounded

444. Inclán, A.: Osteochondrosis of Ischio-Pubic Branch of Hip Bone: Cases, Bol. Soc. cubana de pediat. **12**:223-234 (June) 1940.

enlargement of the ischiopubic epiphysial zone with change in the density of the trabeculation.

The ischiopubic epiphysis closes between the age of 7 and 9 and not 10 and 12 as ordinarily stated. The time of closure may be delayed in hips with pathologic conditions. Rest in bed for several weeks is usually sufficient to relieve the symptoms. A definite cure follows closure of the epiphysial line.

Osteochondritis Dissecans.—King (D.) and Richards [445] review 26 cases of osteochondritis dissecans of the hip joint reported in the literature and add 2 of their own. The disease is a separate entity and may be diagnosed by the characteristic roentgen appearance. In doubtful cases diagnosis is possible only at the time of operation. The typical location of the sequestrum is on the superolateral aspect of the articular surface of the head of the femur above the ligamentum teres femoris. Clinically the disease is to be considered as a possibility in every young adult with a history of chronic pain in the hip, with a limp or with limitation of motion.

Surgical intervention with ablation of the osteochondritic focus gives definite symptomatic relief and offers the possibility of a permanent cure. The head must be dislocated from the acetabulum for proper visualization and removal of the focus. Because of the possible untoward sequelae which may follow this procedure, operation should be undertaken only after careful consideration.

Osteoarthritis of the Hip Joint.—In the treatment of this common ailment, the surgeon has a choice of a variety of methods, any one of which may possess merit in properly selected cases. Henderson [446] reports on the results secured in the treatment of a series of 77 patients at the Mayo Clinic from January 1926 to December 1937.

Manipulation was performed with the patient under anesthesia in 11 cases. Late results were known in 9, and in 4 of these improvement had been obtained. Drilling of the head and the neck of the femur was done in 28 cases. Twenty-five patients replied to follow-up inquiry. Nine reported improvement, and 4 were markedly relieved. Cheilotomy was done in 4 cases without removal of the proliferations about the acetabulum. Henderson considered this a useless operative procedure. Cheilotomy of the head of the femur and of the acetabulum was performed in 6 cases with definite benefit in 3. Cheilotomy and bone drilling were done in 3 cases. One patient continued to have pain; 1 was improving steadily, and 1 could not be followed. Acetabuloplasty

445. King, D., and Richards, V.: Osteochondritis Dissecans of Hip, J. Bone & Joint Surg. **22**:327-348 (April) 1940.

446. Henderson, M. S., and Pollock, S. A.: Surgical Treatment of Osteoarthritis of Hip Joint, J. Bone & Joint Surg. **22**:923-931 (Oct.) 1940.

was used in 5 cases; 4 patients were slightly or moderately improved. In the 12 cases in which the Whitman reconstruction operation was employed, 6 patients were improved. Arthrodesis was done in 6 cases; 5 patients were followed; all had stable, painless hips.

Henderson concludes that the best results were obtained by arthrodesis, though union was slow, requiring six to nine months. Drilling combined with manipulation gave good results in many cases. Acetabuloplasty and extensive cheilotomy gave excellent results in some.

King (T.) reports the results secured with subtrochanteric osteotomy in 26 cases. Pain was completely relieved for 19 patients and decreased for 2 others. Of the remaining 5, 3 died before the results were known and the other 2 were still under observation.

The author emphasizes the importance of securing a new line of weight bearing to relieve and correct deformity. The osteotomy must be slightly oblique in the frontal plane beginning on the lateral surface of the femur 1 fingerbreadth below the trochanteric tubercle and pass upward and inward parallel to the under surface of the neck of the femur. The bone is usually divided above the lesser trochanter.

Postoperative fixation is secured by traction, the lower fragment being constantly abducted. No plaster is used throughout the aftercare; thus a painful swollen thigh and a stiff knee are avoided. The distal fragment seldom slips outward, and if it does, it may be replaced with the patient under anesthesia. King (T.) deplores the fact that such a useful procedure requires so long a period of immobilization (from twelve to sixteen weeks) to secure union. He does not advocate this operation for patients past 60 years of age. [ED. NOTE: There is need for intensive study of large series of cases of osteoarthritis of the hip joint. Some attempt should be made to classify them on a more satisfactory basis in terms of the criteria and indications necessary to establish a definite method of therapy. It seems that the indication for certain procedures is at the moment haphazardly and arbitrarily drawn and that little has been done in the way of studying each patient in the light of the precise symptom complex and pathologic picture.]

XV. CONDITIONS INVOLVING THE KNEE JOINT

Torn Semilunar Cartilage.—Ferguson and Thompson [447] review 100 cases of internal derangement of the knee and find that in 65 the derangement was due to a tear of the semilunar cartilages. There was a ratio of 31 injuries of the internal cartilage to 1 injury of the external cartilage, and the bucket handle type of tear occurred in almost half the cases.

447. Ferguson, L. K., and Thompson, W. D.: Internal Derangements of the Knee Joint: Analysis of One Hundred Cases with Follow-up Study, Ann. Surg. **112**:454-470 (Sept.) 1940.

There were 31 bucket handle tears, 18 anterior tears, 10 midportion tears and 6 posterior tears. In an additional 13 cases a loose internal semilunar cartilage frequently was associated with a hypertrophied infrapatellar fat pad; in cases of this condition the authors conclude that it is best to remove both the fat pad and the cartilage but that the symptoms are probably more often due to the fat pad than to the loose cartilage.

Vinke [448] agrees with Ferguson and Thompson that the bucket handle tear is the most common type and that the internal cartilage is injured more frequently than the lateral cartilage. In his series there was a ratio of 15 injuries of the internal cartilage to 1 injury of the external cartilage.

No new light that would permit a more accurate preoperative diagnosis has been shed on the subject of symptoms produced by tears of cartilage. The history of pain, effusion and locking of the knee after an injury in which the leg is abducted and externally rotated is presumptive evidence of torn cartilage. The type of tear cannot be differentiated, and in many cases only the diagnosis of internal derangement can be made. Vinke, as well as Ferguson and Thompson, points out that the symptom of locking of the knee is absent in about 30 per cent of the cases of torn semilunar cartilage.

Various roentgen studies of the knee joint were made during 1940 in an attempt to gain accuracy in the diagnosis of injuries of the meniscus. Evans [449] and Krogdahl [450] report their observations with the use of Nordheim's technic. To use this method of examination a padded cone is placed against the side of the knee opposite the meniscus that is to be demonstrated in the roentgenogram. The other end of the cone is placed against the examiner's chest, and the leg is forcibly abducted (or adducted, as the case may be). The basis of this method is that the joint space, which is only a potential space, is opened and a temporary vacuum formed in the joint on the side opposite the cone. This vacuum appears in the roentgenogram as a clear area, and within it can be observed the triangular outline of the meniscus. The roentgen exposure should be made after about five seconds of application of the abducting (or the adducting) force. If a longer time is consumed before exposure, the vacuum will have filled with fluid and the meniscus will not be demonstrated.

Krogdahl found Nordheim's method helpful in making the diagnosis in 4 cases of luxation of the medial meniscus. In 3 of the cases the

448. Vinke, T. H.: Ligamentous and Cartilaginous Injuries of the Knee, J. Med. **21**:23-26 (March) 1940.

449. Evans, W. A., Jr.: Roentgenological Demonstration of True Articular Space, with Particular Reference to the Knee Joint and Internal Semilunar Cartilage, Am. J. Roentgenol. **43**:860-864 (June) 1940.

450. Krogdahl, T.: Roentgenologic Diagnosis of Luxation of the Semilunar Cartilages Without the Use of a Contrast Substance, Acta radiol. **21**:335-342, 1940.

findings were verified at the time of operation. He concludes that if the joint space is at all visible with the use of this method effusion is not present even in the smallest degree.

Evans found that the internal semilunar cartilage could be demonstrated in only 70 per cent of normal knees by the use of Nordheim's method. In the remaining 30 per cent, the true joint space was not revealed. He believes that this method will not always, or even usually, yield conclusive results. Only gross lesions will show up as irregularities in the semilunar cartilage; and since the method cannot be used in the presence of effusion, it is of value only in cases in which the joint is normal or in cases in which there is chronic damage of the semilunar cartilage. The technic may be of value in determining whether ligaments are relaxed, but only after comparison with the ligaments of the opposite knee.

Lindblom [451] briefly reviews roentgen studies of the knee joint and tabulates the various contrast mediums which have been used in the past for such studies. He expresses the opinion that the use of iodized oil and of colloidal thorium dioxide should be condemned because of their irritating qualities. If iodized water-soluble salts in nonirritating form are used as contrast mediums, they are as good for the purpose as air or oxygen. He believes that two mediums should not be used together, since this only adds to the difficulty of diagnosis. The roentgen evidences of a lesion in the meniscus are: (1) contrast filling of a fissure, (2) partial defect of the meniscus, a reduction of its prominence or a blunting of its edge and (3) interposition of meniscal substance.

In 75 roentgen studies of the knee joint, using 9 cc. of a 35 per cent solution of diodrast as the contrast medium, Evans was able to diagnose lesions of the meniscus in 43 cases. Surgical intervention was performed in 27 of the 43 cases, and in 25 the diagnosis was confirmed at operation. By examination of ordinary roentgenograms of the 27 joints with known damage to the semilunar cartilages, Evans discovered the presence of an osteophyte on the margin of the tibia and a narrowed joint space in 24. In all but 1 case the arthrosis (arthronosos; arthritis deformans) was on the side affected by the injury of the meniscus. He concludes that such osteophytes appear several months or years after the initial injury and that the tendency toward their development increases with age. He believes that the arthrosis is secondary to the injury of the meniscus and that by comparison of the affected knee with the normal knee the condition may be demonstrated at an early stage. [ED. NOTE: No new information has been added recently to the knowledge of the management

451. Lindblom, K.: Roentgenographic Symptoms of Meniscal Lesion: Question of Connection Between Meniscal Lesion and Arthrosis, Acta radiol. **21**:274-285, 1940.

of injuries of the semilunar cartilages. All authors agree that early treatment should be conservative, with reduction by manipulation or traction followed by immobilization for six to eight weeks. Surgical intervention is commonly reserved for those cases in which repeated episodes of disability occur or for those in which the initial locking cannot be reduced.]

Ferguson and Thompson observe little difference in end results in their group of cases when they compare the group in which only the torn tags were removed with the group in which the entire cartilages were excised.

Bohlman [452] describes an elaborate program of preparation of the patient for removal of semilunar cartilages. This program includes eradication of foci of infection, a test for wound healing, a test with Burky's toxin and perhaps a preoperative course of treatment with Burky's toxin to raise the immunity to staphylococcic infection, a blood platelet count and a twenty-four hour preparation of the skin. He suggests that local anesthesia should be employed at operation and that high frequency electrocautery but not a tourniquet should be used. He washes out the joints with a solution of procaine hydrochloride or physiologic solution of sodium chloride and finally injects air into the joints to cause compression and hemostasis. [ED. NOTE: This technic seems unnecessarily complicated, although the end results in the 50 cases reported by Bohlman were good.]

Bonadeo Ayrolo [453] describes a clamp which he purchased in Vienna, a small guillotine, a meniscus hook and a separator, which he states are of value in operating on the knee joint.

After surgical procedures for torn semilunar cartilages there is frequently a period of disability that lasts for six months to one year. This is noted by Ferguson and Thompson, but they note also that the disability gradually disappears and that the patient's age and the duration of symptoms have no effect on the operative result. They point out that surgical intervention itself does not produce arthritis but that a persistent disability may be a factor in the production of the disease.

In writing about injuries of the semilunar cartilage, Smith and King [454] describe what they believe to be a hitherto undescribed lesion of the knee joint. The symptoms of this lesion have their onset with an injury and are similar to those produced by a torn meniscus, except that

452. Bohlman, H. R.: Improved Technic for Removal of Semilunar Cartilage and Postoperative Treatment, J. A. M. A. **115**:2243-2246 (Dec. 28) 1940.

453. Bonadeo Ayrolo, A.: Personal Statistics on the Surgical Treatment of Meniscus Lesions of the Knee from 1933 to the Present: Special Technique and Instruments, Día méd. **12**:866-868 (Sept. 23) 1940.

454. Smith, A. DeF., and King, B. B.: Injury to the Femoral Articular Cartilage by the Medial Meniscus, Surg., Gynec. & Obst. **71**:679-683 (Nov.) 1940.

locking is seldom observed. At the time of operation there is found in the medial condyle of the femur a depressed region which corresponds in position and outline to the anterior end of the medial meniscus. Converging on this region is a pannus of vascular tissue growing in from the margin of the medial condyle. Although Henderson and others have drawn attention to erosion of the condyles that may occur from pressure exerted by a torn semilunar tag, Smith and King believe that theirs is the first description of such a depression without gross evidence of damage to the semilunar cartilage and that the depression is due to a sudden injury to the extended knee by which the meniscus is suddenly pressed against the femoral articular cartilage. Of 10 cases that they have observed, they report 9; in each case the patient was relieved of symptoms by excision of the medial semilunar cartilage.

Tears of the Cruciate Ligaments.—Injuries to the cruciate ligaments are comparatively rare; but when they occur, the anterior ligament is torn more frequently than the posterior. In only 4 of the 100 cases of internal derangement of the knee in the series of Ferguson and Thompson was there an injury of the cruciate ligament, and in 3 of these cases the injury was associated with other pathologic changes in the knee joint. Interestingly enough only 1 of the patients underwent repair of the cruciate ligament, and yet all the patients regained good use of their knees and returned to active sports. This outcome is in line with Vinke's statement that the lateral ligaments are important from the standpoint of stability but that a knee can function well without a cruciate ligament. He advises immobilization for three months followed by the use of a brace for six months as treatment for acute injuries of a cruciate ligament. Surgical intervention is reserved as a last resort, for reconstruction is rarely necessary if the other ligaments and the muscles around the knee are functioning well. [ED. NOTE: By inference it may be said that Ferguson and Thompson would concur in this opinion.]

An interesting method of substituting for a torn anterior cruciate ligament is described by Tees.[455] Through an incision on the anterolateral aspect of the thigh a strip of fascia lata 10 inches (25 cm.) long is turned down and left attached to the tibial tuberosity in front of the head of the fibula. A hole is then drilled through the lateral tuberosity of the tibia, starting at the point of attachment of this fascial strip and emerging in the joint at the tibial spine. A second hole is then drilled through the lateral condyle of the femur and the fascial strip is threaded through the channel in the tuberosity of the tibia and out of the joint through the channel in the lateral condyle of the femur. The free

455. Tees, F. J.: New Method of Repairing the Anterior Crucial Ligament of the Knee, Canad. M. A. J. **42**:214-216 (March) 1940.

end of fascia is then passed through the hole drilled in the head of the fibula and sutured taut. Tees believes this method of repair a valuable one, for it eliminates opening of the knee joint. Passing the fascial strip through the drill channels is difficult but is accomplished by first inserting a strand of wire through the lower channel and grasping it with a laryngologist's alligator forceps that has been passed into the upper drill channel. After the wire is drawn through, the fascial strips can be attached and pulled through. Tees reports 1 case in which the result from this procedure was good.

Osteochondritis Dissecans.—Berkheiser [456] draws attention to multiple lesions, like those of osteochondritis dissecans, that are found in the patella and the condyles of the femur in aged persons with osteoarthritis. These are yellowish gray oval areas of chondromalacia that are well demarcated and may be covered with exfoliating cartilage. Loose bodies may form and result in a cavity with a fibrous tissue base overlying eburnated bone. Microscopically, the loose bodies are similar to those of osteochondritis dissecans as seen in younger persons. The author recommends surgical intervention for those patients whose advanced age is not a contraindication. For those patients for whom operation is not advisable, a period of immobilization is recommended in the hope that the loose bodies will attach to the synovia and the episodes of locking will thereby be reduced in frequency.

Interesting observations on the fate of foreign bodies within a joint are presented by Hultén and Gellerstedt.[457] Minute pieces of cartilage were kept in physiologic solution of sodium chloride at body temperature for several months with only occasional evidence of liquefaction. From this phenomenon they conclude that autolysis plays little or no part in removing blood clots and small cartilaginous pieces from joint cavities. They then injected sterile suspensions of cartilaginous scrapings into knee joints of animals and observed that the foreign particles first migrated to the suprapatellar pouch or to the posterior compartment; they disappeared quickly from the former location and slowly from the latter. The small particles were phagocytosed, and the larger ones were enveloped by synovial cells growing around them. If large pieces were enveloped, the resulting lump in the synovial membrane could not be leveled but could be torn loose as a foreign body. The synovial membrane reacted to the foreign bodies by hyperemia and increase in histiocytes. This reaction was followed by a decrease in histiocytes but an increase in synovial connective tissue. Eventually fibroplastic synovitis

456. Berkheiser, E. J.: Osteochondritis of the Knee in Aged Patients, S. Clin. North America **20**:97-102 (Feb.) 1940.

457. Hultén, O., and Gellerstedt, N.: Loose Bodies in the Knee and Resorption of Worn-Off Cartilaginous Fragments Simulating Dendritic Synovitis, Acta chir. Scandinav. **84**:1-29, 1940.

resulted, which the authors term "synovitis chondrodetritica." This type of synovitis occurs regularly in chondromalacia patellae, osteochondritis dissecans, arthritis deformans and intra-articular fractures. It results in pain, but rest gives relief by reducing the formation of new particles and after even a few days' rest the acute stage of cartilage digestion is over. The authors state that when surgical intervention for these conditions affords relief it does so by eradication of the source of cartilaginous detritus.

Osteomatosis.—Borsotti [458] records the histologic observations in a case of osteomatosis in which total synovectomy and arthrodesis were performed because of extreme pain in the knee. The synovial membrane was the seat of marked hyperplastic reaction with an increase in blood vessels. There was no evidence of inflammatory reaction, either acute or chronic. Loose bodies were palpated that arose from metaplastic ossification of the abundant young connective tissue that was found in the synovial villi. [ED. NOTE: These microscopic observations appear similar to those in the synovitis chondrodetritica of Hultén and Gellerstedt.]

The author believes that from the histologic point of view chondromatosis, osteochondromatosis and osteomatosis are three separate diseases. [ED. NOTE: They are probably all related and differ only in the degree of metaplasia.]

Recurrent Dislocation of the Patella.—Marottoli [459] divides recurrent dislocations of the patella into three types, traumatic, congenital and habitual, according to the definiteness of the traumatic factor and the degree of morphologic change. Bony changes are present in dislocations of the congenital type but are rare in those of the habitual type. Changes in the soft tissue are most common in dislocations of the habitual type; the most frequent change is elongation and relaxation of the patellar tendon with upward displacement of the patella. The author states that reconstruction of the soft tissue and operation on the bone will not cure the condition. In the 5 reported cases he resorted to extirpation of the patella and obtained good results.

Urrutia Urrutia [460] reviews 30 cases of recurrent dislocation of the patella in which the patients were treated by Putti. All the methods of treatment described in the literature were used in treating these patients, who were divided into groups according to treatment; good results were

458. Borsotti, P. C.: Osteomatosis of the Knee: Case, Chir. d. org. di movimento **25**:427-435 (April) 1940.

459. Marottoli, O. R.: Patellectomy in Therapy of Recidivating Dislocations, Bol. y trab. Acad. argent. de cir. **24**:286-313 (June 5) 1940.

460. Urrutia Urrutia, C.: Surgical Therapy of Congenital Luxation of the Patella, Rev. ortop y traumatol. **9**:203-246 (Jan.) 1940.

obtained in each group. The author finds that the best results were obtained in the group in which mixed types of procedures were used according to the pathologic changes observed at the time of operation. He concludes that the incision for repair should be large enough to permit a general view of the field, so that the plan of operative procedure can be changed if the condition observed makes it necessary.

Roberts [461] expresses the opinion that excision of the patella is not of benefit in the treatment of recurrent dislocations, because the remaining tendon of the quadriceps muscle will often become dislocated.

Hereditary Arthrodysplasia.—Hereditary arthrodysplasia is represented clinically by hereditary changes in the knee together with the presence of rudimentary nails. The patella is dislocated outward, and the knee is broad, with an easily palpable intercondylar notch. The quadriceps muscle and tendon are narrow and weak, and although the motions of the knee are normal, active extension is weak.

Venable [462] dissected a knee joint in which the pathologic change had previously been diagnosed as hereditary arthrodysplasia. The most significant finding was congenital absence of the anterior cruciate ligament; all other changes seemed secondary to this. The author believes that the absence of the one cruciate ligament allowed the tibia to rotate externally. This action led to splaying of the quadriceps tendon, lateral dislocation of the patella and resultant hypertrophic change. Bennett and Bauer [463] produced similar changes in rabbits by dislocating the patella outward and suturing it in its new location. No explanation is offered for the dystrophy of the nails which is associated with congenital absence of the anterior cruciate ligament.

Excision of the Patella.—Roberts briefly reviews the history of excision of the patella for fracture and points out that the first of such operations was performed in 1890 by Althmann. Subsequent to that operation there were sporadic reports of similar treatments, and finally a general interest arose in the procedure. The operation, according to the author, now is accepted in England as the most satisfactory method of treatment. It eliminates the irregularities of the articular surface that follow the treatment of fracture of the patella by any other method, and thus it does not predispose to osteoarthritis. Furthermore, recovery is seldom slow and incomplete after excision of the patella.

The secret of success in extirpating a fractured patella lies in the fact that the primary necessity is suturing of the expansions of the tendon

461. Roberts, N.: Excision of the Patella, M. Press **204**:389-391 (Nov. 13) 1940.

462. Venable, J. H.: Structure of the Knee Joint in Hereditary Arthrodysplasia, South. Surgeon **9**:345-350 (May) 1940.

463. Cited by Venable.[462]

of the quadriceps muscle which were torn at the time of injury. The fracture of the patella is only a part of the injury, and provided the expansions are firmly sutured without lengthening the tendon, normal extension power is restored even if the patella is removed.

Roberts points out some of the disadvantages of excision of the patella. The operation removes the protection that the patella offers to the articular surfaces of the knee joint and to the tendon of the quadriceps muscle. However, the advantages of the operation offset the disadvantages, and he recommends its use. Total excision of the patella is recommended for comminuted fracture, but for young men patients suture of the fragments when they are of equal size is the procedure of choice. The removal of one fragment when it is smaller than the other likewise gives good results and has all the advantages of total excision without its disadvantages. Each case should be judged separately.

Roberts believes that good results can be expected from excision of the patella in osteoarthritis when the process involves mainly the patellofemoral articulation. He doubts its advisability for chronic rheumatoid arthritis. Tuberculosis, chronic osteomyelitis, Paget's disease, osteomalacia and traumatic osteochondritis are other indications for the operation.

Rupture of the Tendon of the Quadriceps Muscle.—Rupture of the tendon of the quadriceps muscle occurs by direct or indirect violence, and according to McMaster [464] the rupture occurs at the insertion of the tendon, at the musculotendinous junction, through the belly of the muscle or at the origin of the muscle. In diseased tendons spontaneous rupture may occur.

Conway [465] points out that the pathognomonic sign of a suprapatellar rupture is absence of fulness of the quadriceps pouch. If the rupture is below the patella, there is an upward shift of the patella, and in either case extension of the knee is weak or absent. Good results follow operative repair.

Xanthoma.—Willenegger [466] collected 35 cases of xanthoma of the joints from the literature. In 31 cases the xanthoma was in the knee joint, and in 4 it was in the ankle. In 23 of the cases the xanthoma was a solitary tumor; in 7 cases the growth was diffuse; in 2 there were multiple tumors, and in 3 the solitary and the diffuse type were combined.

464. McMaster, P. E.: Tendon and Muscle Ruptures: Clinical and Experimental Studies on Causes and Location of Subcutaneous Ruptures, J. Bone & Joint Surg. **15**:705-722 (July) 1933.

465. Conway, F. M.: Rupture of the Quadriceps Tendon with Report of Three Cases, Am. J. Surg. **50**:3-16 (Oct.) 1940.

466. Willenegger, H.: Intra-Articular Xanthomas with Special Reference to Knee Joints, Deutsche Ztschr. f. Chir. **253**:97-124, 1940.

To these cases from the literature the author adds 3 cases of solitary xanthoma of the knee joint. He describes the microscopic structure of the tumors and calls one of them a "xanthoma variant" because of the presence of giant cells. [ED. NOTE: Giant cells are a part of the picture of xanthoma but are not always present. The fact that they are present should not change the diagnosis of xanthoma.]

Cederlund [467] reports 2 cases of xanthoma of the knee. The symptoms and findings of this type of growth are summed up as (1) palpable or visible tumor medial to the apex of the patella, (2) pain, (3) hydrops [ED. NOTE: Yellowish brown or chocolate-colored fluid may be found by aspiration.] and (4) functional disturbances such as locking or impaired motion. The author states that increased blood cholesterol has been reported as present in only half of the cases. [ED. NOTE: Galloway, Broders and one of us (R. K. G.[468]) point out that there is usually a disturbance in the ratio of cholesterol to cholesterol esters in patients with xanthoma.]

Cederlund states that in only 1 of 40 cases was diagnosis of xanthoma made preoperatively and that the growth in this 1 case was a recurrent tumor. Xanthoma usually is diagnosed as loose body, torn cartilage, lipoma or osteochondroma. All authors agree that it is benign, even though Willenegger describes 1 case in which the tumor tissue infiltrated between the cartilage and the bone of the femur. Metastasis from xanthoma has not been recorded.

Cysts of Semilunar Cartilages.—Kulowski [469] reports 19 cases of cyst in the meniscuses of the knee and reviews the theories of causation. He states that the cardinal point in diagnosis is the movement of the mass with the tibia in flexion and in extension. The mass moves on a level with the line of the joint, and the cyst is most prominent on complete extension. The author reports 3 cases of malformed meniscus associated with cyst and states that the number of cases of cyst of the semilunar cartilage reported previous to 1940 is 276.

King [470] reports that in his previous papers he concluded that the process of formation of a cyst in the meniscuses was not degenerative because the cells were well developed in the mucoid area, the nuclei did

467. Cederlund, H.: Two Cases of Intra-Articular Xanthoma in the Knee, Acta chir. Scandinav. **84**:143-154, 1940.

468. Galloway, J. D. B.; Broders, A. C., and Ghormley, R. K.: Xanthoma of Tendon Sheaths and Synovial Membranes: Clinical and Pathologic Study, Arch. Surg. **40**:485-538 (March) 1940.

469. Kulowski, J.: Meniscus Cyst of the Knee Joint, J. Missouri M. A. **37**: 503-508 (Dec.) 1940.

470. King, E. S. J.: Formation of Ganglia and Cysts of Menisci of Knee: Observations on Golgi Apparatus, Surg., Gynec. & Obst. **70**:150-156 (Feb.) 1940.

not indicate a degenerative process and there were droplets of secretion in the cytoplasm of the cells. By special staining of the Golgi apparatus in freshly collected operative specimens, the author found that there was hypertrophy of the cellular structure. He concludes that a cyst of this type is formed by excess secretion and is therefore the result of overactivity and not the result of a degenerative process.

Synovectomy.—Carruthers [471] reviews the history of synovectomy and reports 34 such operations performed on 28 patients. Two of the bilateral operations were performed for chronic hypertrophic villous arthritis, and 4 were done for chronic arthritis. Eight of the unilateral operations were done for chronic synovitis, and the remaining 14 were performed for chronic infectious arthritis. The ages of the patients varied from 18 to 69 years, with the greatest number in the age group of 30 to 40 years. The operation consisted of removal of all the diseased layers of the synovial membrane together with removal of the infrapatellar fat pad and of the meniscuses when they were involved. Traction was applied for ten days, but motion to the point of pain was started forty-eight hours after operation. The author states that synovectomy is a useful operation, and in his group of cases 75 per cent of the patients experienced marked relief from symptoms. Pain and discomfort always were relieved; the average gain in motion was at least equal to what it was before surgical intervention, and in 50 per cent of the cases it was greater. More than 75 per cent of the patients showed general improvement in the arthritis, but whether this relief was due to removal of a focus of infection could not be determined. In 4 of the author's cases ankylosis resulted.

Ankylosis.—Elkins [472] describes an apparatus for forcibly flexing the knees of patients who have fibrous ankylosis in extension. The toes are held to the floor by straps, and a bar fits across the popliteal spaces. The knees are gradually flexed by lowering the body weight. The apparatus is easily constructed and can be built across a door frame.

The late Willis Campbell [473] reported 2 cases in which arthroplasty of the knee was performed with vitallium plates fitted over the lower end of the femur. The results were considered disappointing, possibly owing to the creation of too narrow a joint space, which the author felt should have been ¾ inch (2 cm.). He reported that he was devising a

471. Carruthers, F. W.: Synovectomy of the Knee Joint, South. M. J. **33**:550-552 (May) 1940.

472. Elkins, E. C.: Simple Device for Forced Flexion of the Knee, Arch. Phys. Therapy **21**:468-469 (Aug.) 1940.

473. Campbell, W. C.: Interposition of Vitallium Plates in Arthroplasties of the Knee: Preliminary Report, Am. J. Surg. **47**:639-641 (March) 1940.

plate to cover the upper end of the tibia rather than the lower end of the femur, but at the time of his report he had not used the plate in any case.

Flexion Deformities.—Preston [474] describes a technic for transplantation of the attachment of the patellar tendon in cases of flexion deformity of the knee. The flexion deformity must be corrected first, after which the attachment of the tendon is transplanted distally ⅛ inch (0.32 cm.) for each degree of fixed flexion deformity. The author claimed that by means of a double dovetail at the point of transplantation, active motion could be started immediately after operation.

Chandler [475] reports that because he had difficulty in maintaining the position of the transplanted block of bone he devised a new operative procedure. The patella is transfixed by wire on heavy braided silk and is wired into a normal position with the joint by passing the other end of the wire through a hole drilled beneath the tubercle of the tibia. Narrow strips of the anterior portion of the patellar tendon then are elevated and used to lace through the redundant margins of the tendon. The author believes that this operation reestablishes the normal leverage of the patella by a procedure less extensive and shorter than other methods. It eliminates the possibility of arrest of growth in the epiphysis of the tibia, and the patellar tendon is increased in size and strength by the plication.

New Operations and Technics.—Resection of the Knee Joint: Heyn [476] describes a new technic for resection of the knee. The surfaces of the femur and the tibia are fitted together by a curved osteotomy, and the patella is then countersunk as a graft across the joint. The patella is shaped more or less like a keystone wedge.

Dogliotti [477] describes the use of a portion of the upper end of the tibia as a graft across the resected knee joint. The articular surfaces of the femoral condyles are removed, and the lateral portions of the articulating surfaces are resected. The central portion of the tibial surface is freed but left attached by the cruciate ligaments This piece of bone then is swung around and inserted into a groove anteriorly across the joint line. The author believes that a graft of this type will prove more efficient as a result of unimpaired circulation through the vessels in the cruciate ligaments than grafts of other types. He advises

474. Preston, R. L.: Immediate Restoration of Active Extension of Knee Following Flexion Deformities, Am. J. Surg. **50**:303-305 (Nov.) 1940.

475. Chandler, F. A.: Patellar Advancement Operation: Revised Technique, J. Internat. Coll. Surgeons **3**:433-435 (Oct.) 1940.

476. Heyn, W.: Technique of Resection of the Knee, Zentralbl. f. Chir. **67**: 110-113 (Jan. 20) 1940.

477. Dogliotti, A. M.: New Method for Intra-Articular Arthrodesis of the Knee, J. Internat. Coll. Surgeons **3**:103-106 (April) 1940.

its use for treatment of paralytic dangling knee, spastic knee and early tuberculosis with the central area of the knee joint unaffected.

Exposure of the Knee Joint: Mader [478] describes a technic of exposure of the knee joint in which the patella is resected. Studies on 20 cadavers failed to show any effect on extension of the knee when the patella was removed. [ED. NOTE: This seems a rather drastic procedure to advise in most cases of arthrotomy of the knee. The increase in the number of authors recommending removal of the patella for various reasons would seem to indicate, however, that the patella is not vital to function of the knee joint.]

XVI. CONDITIONS INVOLVING THE FOOT AND ANKLE

Foot Imbalance in Children.—Observation of a large number of cases leads Bloxsom [479] to conclude that the child's foot develops most rapidly between the ages of 1 and 4 years. Some children continue in the nondevelopmental stage, and their feet do not respond to corrective measures. [ED. NOTE: This seems a broad statement, since it is well known that the rate of development is not the same in all persons. Only observation over a number of years will demonstrate the accuracy or error of this statement.] The importance of overweight as the cause of distortion of the ankle and the foot in young children is emphasized by Caldwell.[480] He urges dietary measures and the use of corrective shoes in cases in which overweight is a factor.

Foot Strain and Painful Feet.—Steindler [481] discusses the causation of flatfoot and stresses that the muscles are first relaxed before there can be relaxation of the ligaments and depression of the arch. [ED. NOTE: The question of whether faulty architecture precedes the relaxation and the giving way of the supporting muscles due to overwork or whether the faulty architecture follows the giving way of the muscles is still debatable. The preponderance of evidence seems to indicate that faulty architecture is the primary cause and muscle relaxation secondary.] Cozen [482] stresses the importance of manipulation in the treatment of painful conditions of the feet. The manipulations recommended are in the direction of supination, pronation, dorsiflexion,

478. Mader, V. O.: New Approach to the Knee Joint, Canad. M. A. J. **42**: 17-18 (Jan.) 1940.

479. Bloxsom, A.: Study of Feet of Infants and Children, Am. J. Dis. Child. **59**:45-47 (Jan.) 1940.

480. Caldwell, G. A.: Overweight as Cause of Knee and Ankle Deformities in Babies, Tri-State M. J. **12**:2426 (Feb.) 1940.

481. Steindler, A.: Anatomical and Physiological Conditions of Feet, Mil. Surgeon **86**:379-383 (April) 1940.

482. Cozen, L.: Foot Strain: Simple Method of Treatment, Mil. Surgeon **86**:290-292 (March) 1940.

plantar flexion and rotation. These manipulations are followed by simple balancing of the sole of the shoes in various ways. [ED. NOTE: While unquestionably beneficial in cases in which the condition is mild, it seems doubtful whether manipulation can be expected to accomplish much in symptom-producing conditions of the feet with faulty architecture.] Arkin [483] reports excellent results obtained by the use of Whitman foot plates. [ED. NOTE: Although excellent results are being obtained by the use of rigid plates, supports made of more resilient material, such as sponge rubber, leather or celluloid, are today largely replacing metal supports. They are less difficult to adjust and on the whole more comfortable while just as efficient.]

Operative Correction of Flatfoot.—There seems to be a definite trend toward surgical intervention in the correction of flatfoot, if the condition fails to respond to well directed conservative treatment. White [484] advocates the correction of flatfoot by two osteotomies. One of these is performed on the medial border of the foot for the purpose of shortening this border; the other is performed on the lateral border of the foot for the purpose of lengthening that border. White reports excellent results. [ED. NOTE: While residual anomalies of the feet which fail to respond to treatment frequently require arthrodesing types of operations, it is well to avoid these if possible. The method of White, which does not enter any joint, seems to be a step away from such arthrodesing operations. It is well to bear in mind that many unbalanced feet can be corrected without operation on any bone by means of the methods of Lowman [485] and Young,[486] which are based on bringing about an alteration in the action of the tendon of the tibialis anterior muscle.] These operations are discussed by Burke [487] in a thorough way.

Morton's Toe.—The formation of a neuroma on the fourth plantar digital nerve is suggested by Betts [488] as the cause of Morton's toe on the basis of 1 case observed. [ED. NOTE: Dudley Morton has suggested that the irritation of this nerve might well be the cause of metatarsalgia. Since metatarsalgia does not always affect the same toe, it still seems

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483. Arkin, A. M.: Results of Treatment of Weak Foot by Whitman Plates, M. Rec. **152**:392-393 (Dec. 4) 1940.

484. White, J. W.: Congenital Flat Foot: New Surgical Approach, J. Bone & Joint Surg. **22**:547-554 (July) 1940.

485. Lowman, C. L.: An Operative Method for Correction of Certain Forms of Flatfoot, J. A. M. A. **81**:1500-1502 (Nov. 3) 1923.

486. Young, C. S.: Operative Treatment of Pes Planus, Surg., Gynec. & Obst. **68**:1099-1101 (June) 1939.

487. Burke, G. L.: Surgical Treatment of Flat Feet, Canad. M. A. J. **43**: 327-331 (Oct.) 1940.

488. Betts, L. O.: Morton's Metatarsalgia Neuritis of Fourth Digital Nerve, M. J. Australia **1**:514-515 (April 13) 1940.

reasonable to explain this syndrome by pressure on the digital nerves between the heads of the metatarsal bones when the transverse arch is depressed or reversed.]

Hallux Valgus.—Hallux valgus is a comparatively common and frequently incapacitating and painful condition. McElvenny and Thompson [489] report 100 cases of simple exostosectomy for the relief of this condition. A bunion can occur without hallux valgus. When this situation exists, simple excision of the exostosis is all that is necessary. When hallux valgus is associated with enlargement of the joint of the great toe, correction of the lateral deviation of the great toe is necessary for a successful result. Several types of suggested operations are available for the correction of hallux vulgus, of which the Keller or Schanz operation is probably the best.[490] [ED. NOTE: It should be borne in mind that when pes varus of the first metatarsal bone is present, this condition must be corrected as well as the valgus position of the great toe, and for this type of case the operation of Lapidus [491] seems the procedure of choice.]

Hallux Rigidus.— Hallux rigidus or dorsal bunion is a condition which causes considerable discomfort in walking and at times is definitely incapacitating. The causation of this condition is obscure, but fundamentally it is due to faulty weight bearing from various causes.[492] A variety of procedures is suggested for the relief of hallux rigidus. Several conservative procedures are outlined for the relief of the condition, including the wearing of a heavy-soled shoe and a metatarsal bar.[493] Several surgical procedures are offered, one of which includes reshaping of the metatarsal heads and resection of the proximal end of the first phalanx of the great toe, that is, the Keller operation. Ankylosing the joint of the great toe in 15 degrees of dorsiflexion is suggested by Thompson and McElvenny.[494] [ED. NOTE: The latter suggestion does not recommend itself greatly because the cockup position of the toe would be likely to cause the tip of the shoe to press against the nail,

489. McElvenny, R. T., and Thompson, F. R.: Clinical Study of One Hundred Patients Subjected to Simple Exostosectomy for Relief of Bunion Pain, J. Bone & Joint Surg. **22**:942-952 (Oct.) 1940.

490. Schein, A. J.: Keller Operation: Partial Phalangectomy in Hallux Valgus and Hallux Rigidus: Report of Fifty-Five Operations in Thirty-Two Cases, Surgery **7**:342-355 (March) 1940.

491. Lapidus, P. W.: Operative Correction of Metatarsus Varus Primus in Hallux Valgus, Surg., Gynec. & Obst. **58**:183-191 (Feb.) 1934.

492. Jack, E. A.: Etiology of Hallux Rigidus, Brit. J. Surg. **27**:492-497 (Jan.) 1940.

493. Allan, F. G.: Hallux Valgus and Rigidus, Brit. M. J. **1**:579-581 (April 6) 1940.

494. Thompson, F. R., and McElvenny, R. T.: Arthrodesis of First Metatarsophalangeal Joint, J. Bone & Joint Surg. **22**:555-558 (July) 1940.

and, furthermore, it seems likely that the angle of dorsiflexion would tend to increase as time goes on, resulting in increased pressure on the tip of the toe.] Lapidus [495] describes an extensive operation which is necessarily complex to meet comparatively simple conditions. Remodeling of the tarsal heads and resection of a segment from the base of the first phalanx usually give satisfactory results and seem to comprise the operation of choice.

Hammer Toe.—Congenital hammer toe usually involes the fifth toe. The condition can be very troublesome. It is recommended that its correction be brought about by capsuloplasty and transplantation of the tendon of the extensor muscle of the fifth toe into the metatarsal head.[496] [ED. NOTE: The fifth toe can be amputated without disturbing the architecture of the foot, and since this procedure is simple and effective, it seems more logical to carry out simple amputation than to do such a complicated operation as recommended.] Taylor [497] recommends the passing of a Kirschner wire down through the proximal and midphalanges to maintain the position of the bones after arthrodesis of the first interphalangeal joint in the correction of hammer toe. [ED. NOTE: This method of fixation recommends itself by its simplicity, but it is perhaps not as simple as it seems. Adequate fixation can be secured by a small molded metal splint to permit early use of the feet after operation for the correction of hammer toe, and the advisability of the additional procedure of introducing a wire for fixation is questionable.]

Talipes Cavus.—The evidence presented by Brewster and Larson [498] clearly points out that the best results can be expected from treating feet affected by talipes cavus by triple arthrodesis and transplantation of the long tendons of the extensor muscles of the toes to the necks of the metatarsal bones. Cole,[499] on the other hand, recommends a method of treatment which consists of transplanting the long tendons of the extensor muscles of the toes into the cuneiform bones so that their pull will aid the tibialis anterior muscle in dorsiflexing the ankle. Brewster and Larson state that for the relief of cavus, callus, pain and to a certain extent cockup toes, a triple arthrodesis alone is efficient.

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495. Lapidus, P. W.: "Dorsal Bunion:" Its Mechanics and Operative Correction, J. Bone & Joint Surg. **22**:627-637 (July) 1940.

496. Lantzounis, L. A.: Congenital Subluxation of Fifth Toe and Its Correction by Periosteocapsuloplasty and Tendon Transplantation, J. Bone & Joint Surg. **22**:147-150 (Jan.) 1940.

497. Taylor, R. G.: Operative Procedure for Treatment of Hammer-Toe and Claw-Toe, J. Bone & Joint Surg. **22**:608-609 (July) 1940.

498. Brewster, A. H., and Larson, C. B.: Cavus Feet, J. Bone & Joint Surg. **22**:361-368 (April) 1940.

499. Cole, W. H.: Treatment of Clawfoot, J. Bone & Joint Surg. **22**:895-908 (Oct.) 1940.

This operation when done for claw foot must bring about the following results: (1) The astragalus must be reshaped to elevate the forefoot, so as to flatten the arch; (2) the os calcis must be relieved of its calcaneus position and set back to reduce contracture and increase leverage of the tendo achillis, and (3) the foot must be shortened, to relax the tightness of the plantar fascia and also to lessen the cockup position of the toes by relaxing the contracted tendons. These authors describe a modification of the usual triple arthrodesis to accomplish these objectives better. Cole further states that if bone deformity of marked degree exists, the removal of an anterior tarsal wedge of bone is indicated. This is removed anterior to the midtarsal joint through the cuneiforms, scaphoid and cuboid, thereby preserving the lateral motion of the foot and correcting the deformity. [ED. NOTE: These reports of the treatment of patients with talipes cavus are excellent and come from reliable sources. The original articles should be read.]

Sesamoid Bones.—Miller and Arendt [500] report 3 cases in which there was aseptic necrosis of the head of the first metatarsal bones. They consider that the causative factor was concentration of weight bearing on the head of the metatarsal bones due to backward displacement of the sesamoid bones. The effect of such backward displacement of the sesamoid bones is to deprive the head of the first metatarsal bone of the protection which these bones normally give it and to allow the head of the bones to be subjected to repeated trauma. The conservative treatment suggested is the use of a metatarsal bar and, failing that, removal of part of the proximal phalanx of the great toe (Keller operation). [ED. NOTE: The condition described may be a definite entity, but it strikingly resembles hallux rigidus in appearance and effect.]

March Fractures.—Hansen [501] and Drummond [502] discuss march fractures. Hansen recommends treatment by a heavy-soled shoe or a plaster cast. [ED. NOTE: There is nothing particularly new in either of these articles.]

Trench Foot and Frost Bite.—Greene [503] discusses the causation and the treatment of trench foot. The causative factors, in his opinion, are slowing of the circulation and decrease in the oxygen tension. He suggests the wearing of properly fitting, dry footwear as a prophylactic

500. Miller, L. F., and Arendt, J.: Deformity of First Metatarsal Head Due to Faulty Foot Mechanics, J. Bone & Joint Surg. **22**:349-353 (April) 1940.

501. Hansen, H.: Hints About Marching Feet, Mil. Surgeon **86**:592-593 (June) 1940.

502. Drummond, R.: March Fracture: Report on Case Involving Both Feet, Brit. M. J. **2**:413-414 (Sept. 28) 1940.

503. Greene, R.: Frost-Bite and Trench Foot, Lancet **1**:303-305 (Feb. 17) 1940.

measure, and he advises against applying heat and rubbing with snow. He suggests protection of the feet and general supportive measures, including rest and warm drinks.

Sprained Ankle.—The treatment of sprained ankle is discussed by several authors. The recommendations vary from simple strapping to extensive use of cold, injections of 2 per cent procaine hydrochloride, use of crutches and massage.[504] [ED. NOTE: It seems well established that adequate support by proper strapping, use of sinusoidal current and early resumption of function give satisfactory results in the majority of cases.]

Shoes.—Several timely articles are devoted to the qualities necessary to a proper shoe.[505] [ED NOTE: Unfortunately, there is a definite lack of understanding on the part of physicians of what constitutes a proper shoe and a widespread feeling that the so-called corrective shoe can be recommended on the basis of the claims made by the manufacturer. Improved management of painful conditions in the feet can be anticipated only when physicians familiarize themselves with correct shoeing of the feet and learn that the so-called corrective shoe does not solve the problem of the patient with a symptom-producing foot condition.]

XVII. CONDITIONS INVOLVING THE SHOULDER, NECK AND JAW

Torticollis.—Koster [506] reports 2 cases of spasmodic torticollis, which is recognized as being stubborn to all forms of treatment. He obtained good results by using large doses of atropine, 3.25 to 8.75 mg. daily. Rugh [507] believes that spasmodic torticollis is of two main types: one of psychogenic origin and one due to lesions in the brain stem. Over a long period of years he has used plaster fixation of the head followed by support in a brace with satisfactory results. Whiles [508] stresses that most patients with torticollis are also afflicted with underlying anxiety and social maladjustment. He has had good results with psychotherapy

504. Galland, W. I.: Adhesive Strapping for Sprain of Ankle, J. Bone & Joint Surg. **22**:211-215 (Jan.) 1940. Alexander, H. H., Jr.: Treatment of Sprained Ankle, Am. J. Surg. **50**:581-584 (Dec.) 1940. Ball, C. R.: Sprained Ankles: Treatment by Novocaine and Adrenalin Injections, U. S. Nav. M. Bull. **38**:499-502 (Oct.) 1940.

505. Armstrong, G. W.: Treatment of Painful Feet, Canad. M. A. J. **42**:227-231 (March) 1940. Lake, N. C.: The Foot and the Shoe, M. Press **203**:220-224 (March 13) 1940. Jones, A. R.: Shoes and Disabilities of Feet, ibid. **203**:224-226 (March 13) 1940.

506. Koster, S.: New Guiding Principles for Treatment of Torticollis Spastica (Cerebralis), Nederl. tijdschr. v. geneesk. **84**:225-230 (Jan. 20) 1940.

507. Rugh, J. T.: Spasmodic Torticollis: Its Cause and Treatment, Am. J. Surg. **49**:490-495 (Sept.) 1940.

508. Whiles, W. H.: Treatment of Spasmodic Torticollis by Psychotherapy, Brit. M. J. **1**:969-971 (June 15) 1940.

supplemented with physical therapy in the treatment of these conditions. [ED. NOTE: The forms of treatment of spasmodic torticollis are still varied. Psychotherapy, physical therapy, immobilization in a plaster cast or a brace, drug therapy and operation have all produced good results in some cases. Each case must still be studied as an individual problem and treatment decided on accordingly.]

Occasionally torticollis is compensatory. This is exemplified in McCullough's [509] case, in which there was a spasm of unknown cause in the inferior oblique muscle of one eye. The patient, a child of 6, tilted the head to correct diplopia. Tenotomy of the muscle relieved both the diplopia and the torticollis.

Treatment of congenital torticollis is well covered by Soeur [510] in a report of 20 cases, with excellent results in 19. He stresses correction of the contracture, minimum operative risk and avoidance of visible scars. For correction in patients under 14 years of age, both ends of the sternocleidomastoid muscle are severed. Local anesthesia is frequently employed. In bipolar tenotomy the author has found subcutaneous tenotomy of the clavicular attachment satisfactory; he advocates immobilization in a plaster cast for two months after operation. [ED. NOTE: The open method is still the procedure of choice. In many clinics the application of traction or of sand bags followed by early physical therapy is replacing the use of the plaster cast for postoperative immobilization.]

Injuries and Diseases of the Shoulder.—Nathanson [511] stresses the importance of complete physical examination of patients with pain in the shoulder. He reports 3 cases in which the symptoms in the shoulder with less careful examination might have been diagnosed as bursitis of the shoulder; further examination revealed a neoplasm in the pulmonary apex in 2 cases, and in the third case the patient was treated for bursitis with no relief. Later examination revealed an opaque lesion in the upper lobe of the right lung with erosion of the ribs. If such signs as Horner's syndrome are present or if after a reasonable trial treatment has given no relief, the patient should again be given a thorough physical examination.

McKenna [512] believes tendinitis, which may involve any or all the tendons, but principally affects those of the supraspinatus muscle and

509. McCullough, M. K.: Spasm of Inferior Oblique with Head Tilt, Texas State J. Med. **36**:507-510 (Nov.) 1940.

510. Soeur, R.: Treatment of Congenital Torticollis, J. Bone & Joint Surg. **22**:35-42 (Jan.) 1940.

511. Nathanson, L.: Pulmonary Apical Tumefaction Simulating Bursitis: Necessity for Routine Chest Examination for Patients with Shoulder Pain, New York State J. Med. **40**:860-864 (June 1) 1940.

512. McKenna, D. E.: Tendinitis of Shoulder, M. Times, New York **68**:259-268 (June) 1940.

long head of the biceps brachii muscle, is the primary lesion in most disabilities of the shoulder. He states that this is the result of excessive use, wear and tear, resulting in fibrillation, saponification and calcareous degeneration. The subacromial bursa is only secondarily involved.[513] Irrigation, as recommended by Patterson and Patterson,[513a] is the accepted form of treatment for definite subacromial bursitis. In the presence of acute subacromial bursitis, especially with calcification, Bartels [514] feels that operation is necessary and that the calcareous deposit should be removed with a curet.

According to Kendrick,[515] periarthritis frequently follows subacromial bursitis as the result of trauma. When this occurs, rest in bed is often indicated, although needling or irrigation, as Weeks [516] also suggests, may give prompt relief from pain. Restoration of function should be the aim of all therapy. When the disease is quiescent and limitation is due to mature adhesions, with the patient under anesthesia the arm should be carefully brought into abduction and full elevation; then traction of 3 to 5 pounds (1.3 to 2.3 Kg.) should be applied to hold the arm in abduction and external rotation. This should be followed by physical therapy and active exercise; the arm should always be returned to a position of rest in full elevation and abduction until there is full passive motion without pain. This position can also be secured by slowly stretching with traction when manipulation is contraindicated. This treatment is the same as that suggested by McKenna.[512]

After working with cadavers, Martin [517] makes an interesting statement about rupture of the supraspinatus muscle. He finds that the position of the humerus is the same whether the arm is carried into the upright position through the coronal or through the sagittal plane. Thus the humerus must rotate 180 degrees when the arm is elevated in the coronal plane. In this upright position the muscles inserted in the region of the bicipital sulcus are twisted around the surgical neck. It follows that if the arm is accidentally forced upward in the coronal plane while preventing lateral rotation of the humerus, one of four things happens: (1) The head of the humerus is dislocated; (2) the insertion of the tendon of the supraspinatus muscle is lacerated; (3) the acromial

513. (*a*) Patterson, R. L., Jr., and Patterson, R. H.: Further Observations on Treatment of Bursitis of the Shoulder, Am. J. Surg. **49**:403-408 (Sept.) 1940. (*b*) McKenna.[512]

514. Bartels, W. P.: Surgical Treatment of Acute Subacromial Bursitis, J. Bone & Joint Surg. **22**:120-121 (Jan.) 1940.

515. Kendrick, J. I.: Physical Therapy Principles of Periarthritis of Shoulder, Arch. Phys. Therapy **21**:41-44 (Jan.) 1940.

516. Weeks, A.: Subdeltoid Bursitis, Arch. Surg. **41**:554-556 (Aug.) 1940.

517. Martin, C. P.: Movements of Shoulder Joint with Special Reference to Rupture of Supraspinatus Tendon, Am. J. Anat. **66**:213-234 (March) 1940.

process is fractured, or (4) the greater tuberosity of the humerus is torn off. Lateral rotation is due partly to the action of the deltoid muscle, partly to the pull of the supraspinatus muscle and partly to the eccentric position of the coracoacromial arch.

The Nicola operation still seems to be the procedure of choice for recurrent dislocation of the shoulder, although Orell [518] has developed a technic in which a piece of os purum is implanted on the anterior rim of the glenoid cavity with a specially designed osteoperforator. According to Orell the operation is simple and can be performed quickly. Magnuson and Stack [519] report a familial incidence of recurrent dislocation of the shoulder; the condition was bilateral in twins and unilateral in their father, a brother and an uncle. [ED. NOTE: This is most unusual.]

Lieberman [520] reports a case of the unusual condition of subluxation of the long head of the biceps from the bicipital groove. The patient was completely relieved of all symptoms by a Nicola operation.

Watson [521] reports a new technic for taking a superior view roentgenogram of the shoulder showing the end of the clavicle and the spine of the scapula. The patient stands erect with the right side to the film; the right arm is extended forward and the left arm at the side. The roentgen tube is at a distance of 6 feet (180 cm.) and is directed downward from above at an angle of 45 degrees. [ED. NOTE: A new technic for taking roentgenograms to show a different view of a joint is always welcome news to the surgeon.]

In cases of acromioclavicular dislocation, Murray [522] advocates the insertion of a Kirschner wire through the acromion into the clavicle. In the 5 cases he reports the results were excellent. The patients returned to work a few days after insertion of the wire. In 2 cases, wires were inserted from the coracoid process into the clavicle with equally good results. Removal of the wire is optional, since it produces no evidence of irritation. [ED. NOTE: The efficiency of this procedure is debatable. One of us (H. E. C.) has seen infection occur after this operation. It certainly should not be considered a routine procedure but should be used only in selected cases.]

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518. Orell, S.: Surgical Treatment of Recurrent Dislocation of Shoulder Joint, Surg., Gynec. & Obst. **70**:945-947 (May) 1940.

519. Magnuson, P. B., and Stack, J. K.: Bilateral Habitual Dislocation of Shoulder in Twins: Familial Tendency, J. A. M. A. **114**:2103 (May 25) 1940.

520. Lieberman, H. S.: Traumatic Subluxation of Long Head of Biceps Brachii: Case Report, J. Bone & Joint Surg. **22**:425-428 (April) 1940.

521. Watson, W.: Abnormal View of Shoulder, Radiography **6**:76-77 (April) 1940.

522. Murray, G.: Fixation of Dislocations of Acromioclavicular Joint and Rupture of the Coracoclavicular Ligaments, Canad. M. A. J. **43**:270-271 (Sept.) 1940.

Rupture or tear of the long head of the biceps or of its radial attachment is rare except in the aged. Good results are reported by Kraus,[523] Schrader [524] and McKee [525] from operative repair, which should always be the method of choice.

Bosworth [526] reports most accurately the anatomic findings in 28 cases of chronic disability of the shoulder. He classifies these according to whether there is present: (1) no pathologic lesion, (2) a lesion of a tendon, (3) a bursal lesion or (4) an exostosis. He finds that an anterior incision in the deltoid muscle with division of the muscle fibers at the acromion gives an excellent exposure and leaves no functional defect. [ED. NOTE: This report should be carefully studied by all who perform operations on the shoulder.]

Cleaves [527] reports a case of apophysitis of the acromion in which there was an irregular appearance similar to that found in the os calcis when it is affected by the same condition. It followed trauma. All symptoms subsided within a year.

Cervical Rib and Scalenus Anterior Muscle Syndrome.—Aynesworth [528] has coined the term "cervicobrachial syndrome" for the mixed symptoms caused by cervical ribs and the scalenus anterior muscle. According to symptoms he divides the patients into three groups: (1) those who exhibit neurologic symptoms as their major manifestation; (2) those who exhibit vascular symptoms as their chief manifestation; (3) those who exhibit a combination of vascular and neurologic symptoms. Trauma [529] is a precipitating cause in a high percentage of cases. As a rule symptoms are much more severe when there is an underlying cervical rib.[529b] Smith [530] reports a case in which there was a thickened

523. Kraus, H.: Traumatic Rupture of Biceps Tendon, Beitr. z. klin. Chir. **171**: 121-125, 1940.

524. Schrader, E.: Avulsion of Superior and Inferior Tendon Insertion of Biceps Brachii, München. med. Wchnschr. **87**:555-556 (May 24) 1940.

525. McKee, G. K.: Spontaneous Rupture of Tendon of Long Head of Biceps Brachii, Brit. M. J. **1**:1018 (June 22) 1940.

526. Bosworth, D.: Analysis of Twenty-Eight Consecutive Cases of Incapacitating Shoulder Lesions Radically Explored and Repaired, J. Bone & Joint Surg. **22**:369-392 (April) 1940.

527. Cleaves, E. N.: Unusual Shoulder Lesion (Osteochondritis of Scapular Acromial Apophyses), J. Bone & Joint Surg. **22**:182-184 (Jan.) 1940.

528. Aynesworth, K. H.: Cervicobrachial Syndrome: Discussion of Etiology with Report of Twenty Cases, Ann. Surg. **111**:724-742 (May) 1940.

529. (*a*) Jelsma, F.: Scalenus Anticus Syndrome—End Results of One Hundred Cases: Report of Five Illustrative Cases, Internat. Clin. **4**:219-225 (Dec.) 1940. (*b*) Donald, J. M., and Morton, B. F.: Scalenus Anticus Syndrome With and Without Cervical Rib, Ann. Surg. **111**:709-723 (May) 1940. (*c*) Aynesworth.[528]

530. Smith, B. C.: Thrombosis of Third Portion of Subclavian Artery Associated with Scalenus Anticus Syndrome, Ann. Surg. **111**:546-548 (April) 1940.

fascia lateral and posterior to the scalenus anterior muscle producing similar symptoms. For the milder forms palliative measures will suffice, but in most cases scalenotomy [529a] or removal of the offending cervical rib [531] is the method of choice.

Kaplan [532] reports injections of 1 per cent solution of procaine hydrochloride into the scalenus anterior muscle giving relief that may be permanent. It is believed that the cervical sympathetic nerves through which the pain is mediated may be paralyzed. There is also a relaxation of the scalenus muscle.

Patterson [533] considers aneurysm of the subclavian artery to be rare. He believes that in the scalenus muscle syndrome pressure is exerted during inspiration on the brachial plexus and the subclavian vessels and that circulatory disturbances are due to constant stimulations of the constrictor nerve fibers going to the artery but that in addition there may be direct pressure on the vessel.

Pain in the Cervical Portion of the Spine.—Neviaser [534] reports a traction-manipulation treatment for stiff neck. It was used on 76 patients, with complete relief for 34, improvement for 19 and no relief for 3. The author recommends first heat and then massage for five minutes followed by heat for twenty minutes more. Traction is now applied by means of a head halter. The patient's heels barely touch the floor; the head is then rotated to stretch the contracted muscles. At the point of maximum rotation a click is often heard, and relief is frequently immediate. This procedure may be repeated the following day. For chronic stiffness of the neck, traction of the head with a 2 to 5 pound (0.9 to 2.3 Kg.) pull may be continued with the patient in bed. [ED. NOTE: This treatment may be dangerous if great care is not exercised in the control of stretching and rotation. It is certainly based on sound reasoning. How lasting the improvement is for this same group of patients and also the number of recurrences should be reported in two to five years.]

Retruded Chin.—In all cases of retruded chin, New and Erich [535] state that there is a disturbance in the function of the jaws with abnormal

531. Silbert, S.: Complete Recovery from Serious Vascular Impairment Following Removal of Cervical Rib, Surgery **7**:392-395 (March) 1940. MacFee, W. F.: Cervical Rib Causing Partial Occlusion and Aneurysm of Subclavian Artery, Ann. Surg. **111**:549-553 (April) 1940.

532. Kaplan, L.: Painful Shoulder: Diagnosis and Treatment, Pennsylvania M. J. **44**:289-297 (Dec.) 1940.

533. Patterson, R. H.: Cervical Ribs and Scalenus Muscle Syndrome, Ann. Surg. **111**:531-545 (April) 1940.

534. Neviaser, J. S.: Traction Manipulation Treatment of "Stiff Neck," M. Ann. District of Columbia **9**:75-77 and 108 (March) 1940.

535. New, G. B., and Erich, J. B.: Retruded Chins: Correction by Plastic Operation, J. A. M. A. **115**:186-191 (July 20) 1940.

dental occlusion. The three types are: (1) retarded mandible due to malocclusion, (2) retruded mandible due to arrested growth in the lower jaw and (3) receding chin not associated with malocclusion. Orthodontic procedures will cure the condition in children if started early enough, but plastic procedures are required for adults. The authors recommend fitting costal cartilage over the symphysis of the mandible in all cases requiring operation. [ED. NOTE: This operation should be done only by a plastic surgeon or by one trained in such procedures.]

XVIII. CONDITIONS INVOLVING THE ELBOW, FOREARM, WRIST AND HAND

Lesion of the Elbow.—De Araujo [536] revives interest in resection instead of amputation or simple drainage as treatment for suppurative and traumatic lesions of the elbow. The high percentage of resulting flail elbows does not discourage him. He describes an arthroplastic operation which succeeded in reestablishing stability in 1 case. Kini [537] reports good results with the use of resection instead of arthroplasty in 9 cases of poorly reduced dislocation of the elbow. He was working in southern India, where his limited facilities made the more complicated operation precarious. [ED. NOTE: Current interest in vitallium must not be allowed to obscure the value of resection of the elbow in selected cases. Resection is still one of the best ways of solving the problem of chronic infection or mechanical derangement of the elbow.]

Burman [538] describes a case in which débridement including resection resulted in a flail elbow. Stability and good function were obtained, and excessive valgus of the elbow was reduced by the insertion of strips of fascia, so placed as to imitate the ligamentum collaterale ulnare.

Slowick [539] reports obtaining good results in 5 cases of epicondylitis of the humerus by injecting sodium morrhuate. Considerable reaction was obtained. A varying number of injections was used, in some cases one and in others three. The writer suggests that after preliminary injection of procaine hydrochloride 0.3 cc. of 5 per cent solution of sodium morrhuate, or even less, should be injected under the tendon of the extensor muscle. In the treatment of ganglions Ball [540] injects

536. de Araujo, A.: Autoplastic Articular Reconstruction of the Unstable Elbow, Rev. brasil. de orthop. e traumatol. **2**:3-15 (Sept.-Oct.) 1940.

537. Kini, M. G.: Dislocation of Elbow and Its Complications: Simple Technique for Excision of Elbow, J. Bone & Joint Surg. **22**:107-117 (Jan.) 1940.

538. Burman, M. S.: Fascial Plastic Operation for the Restoration of the Ulnar Collateral Ligament of the Elbow in Marked Lateral Instability of the Joint After Its Resection, Am. J. Surg. **49**:112-115 (July) 1940.

539. Slowick, F. A.: Sodium Morrhuate in Treatment of Epicondylitis of the Humerus: Report of Five Cases, New England J. Med. **222**:1071-1074 (June 27) 1940.

540. Ball, E. J.: New Treatment of Ganglion, Am. J. Surg. **50**:722-723 (Dec.) 1940.

2 cc. or less of a proteolytic enzyme (carotid) to liquefy the gelatinous material, which can then be freely aspirated. After thirty minutes the enzyme tends to destroy the secretory action of the wall of the ganglion. After aspiration and irrigation with distilled water, a pressure dressing is applied. Recurrence is rare; but if it occurs, he suggests that a few drops of 10 per cent solution of sodium morrhuate be injected.

Lesions of the Forearm.—Boyd [541] describes a surgical approach to the proximal third of the radius and the ulna through one posterolateral incision. It has the virtue of exposing the upper third of the radius and, if necessary, all of the ulna without damaging the radial nerve. The incision is particularly suited to the open reduction of Monteggia's fracture.

Blount [542] advocates osteoclasis of both bones of the forearm to correct the deformity of resistant supination, which cannot be further corrected by other means and which occurs in children after poliomyelitis and obstetric injury to the shoulder. The cosmetic and functional results were good in 7 cases and fair in 2. In addition to avoiding a scar, the method has other advantages over osteotomy, in that the healing period is shorter and there is not the danger of nonunion that must be taken into account when open osteotomy is performed on children with subsequent disturbance of the position of the bone ends.

Volkmann's Ischemic Contracture.—Rouhier and Bosson [543] describe a case in which there were multiple fractures, including one just above the elbow. The latter was complicated by typical Volkmann ischemic contracture which terminated in gangrene of the forearm. This necessitated supracondylar amputation and afforded an opportunity for examination of the arm. Most of the gangrene was on the anteromedial surface of the forearm. Complete liquefaction of the muscles explained the relaxation of the flexion contracture after the first few days. Other muscles appeared healthy. Nerve trunks appeared normal on both macroscopic and microscopic examination. Careful dissection of the brachial artery and of its radial branch revealed no abnormality, and clinical examination of the proximal portion showed it to be normal. At the bifurcation there was a nonadherent clot the size of a large grain of wheat. Beyond the first centimeter into the hand, the ulnar artery was completely thrombosed. Veins were similarly thrombosed. The fracture had not affected the surrounding soft parts.

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541. Boyd, H. B.: Surgical Exposure of Ulna and Proximal Third of Radius Through One Incision, Surg., Gynec. & Obst. **71**:86-88 (July) 1940.

542. Blount, W. P.: Osteoclasis for Supination Deformities in Children, J. Bone & Joint Surg. **22**:300-314 (April) 1940.

543. Rouhier, G., and Bosson, C.: Volkmann's Ischemic Paralysis Terminated by Gangrene and Amputation, Mém. Acad. de chir. **66**:409-415 (April 17-24) 1940.

Luzuy [544] reports 2 cases in which Volkmann's ischemia in an early stage was present after a bullet wound in the forearm and in which the symptoms were relieved by injecting 5 or 6 cc. of a 0.5 per cent solution of procaine hydrochloride into the stellate ganglions. From his personal acquaintance with the work of Leriche, he concludes that in the absence of neural lesions proved by electric stimulation, Volkmann's contracture should be considered to have a vasomotor origin and should be treated by injecting procaine hydrochloride into the stellate ganglion.

Bruce [545] records an instance of localized Volkmann contracture of the middle finger of the right hand following contusion of the volar aspect of the midforearm with a tennis ball. There was isolated involvement of the fibers of the flexor digitorum sublimis muscle to the middle finger. Open elongation of the involved tendon just above the transverse carpal ligament resulted in a "virtually complete restoration, both of appearance and of function."

Jones [546] describes the pathologic changes noted in performing open reduction in a case in which Volkmann's contracture in a child 10 years old was in an early stage. He noted that the bellies of the muscles of the flexor group were blue-black with congestion. The involved fascia was divided. The lumen of the brachial artery was obliterated from 2 inches (5 cm.) above the elbow joint into the radial and ulnar branches. After removal of the tunica adventitia with its sympathetic nerve fibers there was no expansion of the artery in ten minutes, but complete return of circulation occurred later. The operation was performed four hours after the accident. Plewes [547] reports a case to support his contention (to which Jones also subscribes) that the syndrome is produced by occlusion of arteries. The elbow of a girl of 7 was operated on one hour after a compound supracondylar fracture. Well developed Volkmann ischemia was already present. Débridement exposed the brachial artery, which "felt like a piece of string." No pulsation was felt in the radial or ulnar arteries. One inch (2.5 cm.) of the brachial artery was resected. The intima of the excised portion was discolored by subintimal hemorrhage, and there was a small thrombus attached to the wall. The median nerve was swollen and discolored. Five minutes after resection the hand was warm; a feeble radial pulse could be felt at the end of the operation.

544. Luzuy, M.: Ischemic Contractures from Traversing Bullet Wounds of Upper Extremities: Two Cases with Therapy by Procaine Hydrochloride Injection of Stellate Ganglion, Mém. Acad. de chir. **66**:2-5 (Jan. 3-10) 1940.

545. Bruce, J.: Localized Volkmann's Contracture, J. Bone & Joint Surg. **22**: 738-739 (July) 1940.

546. Jones, E. B.: Volkmann's Ischaemia: Observations at Open Operation, Brit. M. J. **1**:1053-1054 (June 29) 1940.

547. Plewes, L. W.: Occlusion of the Brachial Artery and Volkmann's Ischaemic Contracture, Brit. M. J. **1**:1054-1055 (June 29) 1940.

On the day after the operation there was complete median palsy which disappeared within three months. The writer concludes that early arteriectomy prevents the appearance of Volkmann's syndrome and cites 2 cases of Griffiths and 1 of Karusseau. It appears from the literature that after twenty-four hours arteriectomy will not prevent it.

Griffiths [548] presents a masterly discussion of Volkmann's ischemic contracture which brings the subject up to date. In his opinion the syndrome is due to injury of arteries and to accompanying spasm of the collateral circulation. The intravenous use of papaverine is suggested. If this fails, the contused or lacerated portion of the artery should be excised between ligatures.

Surgical Approach to the Wrist Joint.—Smith-Petersen [549] presents a new surgical approach to the wrist joint which is particularly useful in arthrodesing the radiocarpal joint without interfering with pronation and supination. The incision may be extended distally to expose the row of carpal bones.

> The incision starts two and one-half inches above the ulnar styloid running parallel with the ulna to a point just distal to the styloid; it then curves anteriorly in the direction of the proximal end of the fifth metacarpal; the distal portion runs parallel with this bone for a distance of approximately one inch. A bayonet incision of this type results in two flaps, which are easily retracted. Since the incision is over the ulnar aspect of the wrist, the resulting scar is out of sight most of the time.
>
> By a division of the subcutaneous fat and fascia, the ulnar periosteum is exposed and incised. If the surgeon is not in too much of a hurry, a true subperiosteal exposure of the ulna can be obtained.
>
> Following an oblique osteotomy, the distal inch or so of the ulna is removed, exposing the ulnar aspect of the radius. The capsule and the ligaments are reflected from the radius along with the periosteum of the latter, exposing the radiocarpal joint. The same procedure is carried out distally, reflecting capsule and ligaments from the carpus. The increased mobility thus obtained facilitates the complete removal of the cartilage from the radius and the carpus. With the hand in the optimum position of dorsiflexion, slots are cut in the radius and the carpus, into which the graft is sunk. As a rule, the excised portion of the ulna, properly shaped, makes an efficient graft; the remaining fragments are packed around the volar aspect of the graft.

Anatomy of the Wrist.—Salsbury [550] presents a detailed anatomic study of the ulnar bursa based on the dissection of 46 hands. He is particularly interested in the communication between the ulnar bursa and the digital sheath of the little finger. In 25 per cent of the hands there was no communication; in 50 per cent the communication was

548. Griffiths, D. L.: Volkmann's Ischaemic Contracture (Hunterian Lecture), Brit. J. Surg. **28**:239-260 (Oct.) 1940.

549. Smith-Petersen, M. N.: New Approach to Wrist Joint, J. Bone & Joint Surg. **22**:122-124 (Jan.) 1940.

550. Salsbury, C. R.: Contribution to the Anatomy of the Ulnar Bursa, Canad. M. A. J. **43**:430-432 (Nov.) 1940.

small and valvelike. In most of the hands without normal communication the two synovial sacs were separated by only a thin septum. He suggests that the pressure of an infected mass could easily rupture this septum and that this would explain the high percentage of cases in which the communication is recorded. He thinks that infections of the ulnar bursa are likely to reach the digital sheath but that infections of the digital sheath are less likely to spread to the bursa, because of the valvelike arrangement of the ulnar bursa.

Cave [551] discusses the carpus from the developmental and anatomic points of view with special reference to fractures of the scaphoid bone. He reviews the development and blood supply of the carpus. A fracture through the midportion of the bone frequently involves the bifurcation of the main nutrient artery, interrupting the blood supply of the proximal fragment. The distal fragment is nourished by a smaller artery entering the tubercle. The loss of nutrition is an important factor in the production of nonunion in some cases. Cave emphasizes the importance of anteroposterior roentgenograms with the hands in ulnar deviation and oblique views with the hands in midpronation in the diagnosis of this fracture. In a series of 110 injuries of the carpus, fracture of the scaphoid bone occurred 68 times, usually as the result of acute dorsiflexion of the wrist. For fresh fracture he advocates the conventional immobilization of the thumb in a cast with the wrist in 30 degrees of dorsiflexion and 15 degrees of radial deviation until union is roentgenologically demonstrable. Prolonged immobilization is more important than physical therapy, and he suggests the use of a leather wristlet after removal of the cast. Definite roentgen evidence of nonunion after four months is an indication for operative treatment. The writer recommends either a slot or a dowel graft. The technic of the dowel-grafting operation is given as used in the later cases.

Kienböck's Disease.—Erler [552] recommends drilling the affected lunate bone with a 2 mm. spiral drill, which serves to remove some of the necrotic tissue. Prolonged rest is also necessary. Simonetti [553] describes the development of necrosis of the lunate bone in a case in which the wrist was subjected to repeated minor traumas. He suggests the designation of two phases of the malady. In the first there is a roentgenologic picture of nonspecific osseous rarefaction. In the second there is osteosclerosis. He emphasizes the importance of the circulatory factor in causation.

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551. Cave, E. F.: Carpus, with Reference to Fractured Navicular Bone, Arch. Surg. **40**:54-76 (Jan.) 1940.

552. Erler, F.: Therapy of Kienböck's Disease, Ztschr. f. Orthop. **70**:357-360, 1940.

553. Simonetti, C.: Kienböck's Disease: Review of Literature and Report of Case, Ann. di radiol. diag. **14**:59-67 (Feb.) 1940.

Etcheverry [554] reviews the literature and reports 2 cases. He injects the arterial tree of the wrist of an infant to demonstrate the extension of the branches to the scaphoid and semilunar bones. Almost the entire blood supply enters the semilunar bone on the dorsum of the wrist, the site of most trauma. The semilunar bone contains end arteries which cannot be easily replaced if damaged. There are no muscle attachments to act as avenues of entrance for new vessels. Repeated minor traumas are the most likely cause of Kienböck's disease. Caby [555] records the occurrence of bilateral osteoporosis of the carpus with Kienböck's disease in a case of bilateral cervical rib. He feels that the vasomotor syndrome associated with the cervical ribs was more than coincidental in causing the osseous changes.

Loose Body in the Wrist Joint.—A woman 45 years old complained to Michaelis [556] of recurrent attacks of numbness, locking, pain and swelling in the ulnar half of the left wrist. The symptoms were relieved by change of position. Roentgen examination revealed no abnormalities. Operation showed a cartilaginous free body 15 mm. long in the wrist joint. Removal was followed by complete recovery.

Madelung's Deformity.—Horwitz [557] was stimulated by operation on a patient with Madelung's deformity to a detailed anatomic and roentgen study of the wrist joint. After operation he achieved stability in the relaxed and snapping wrist joint by threading half the tendon of the extensor carpi radialis brevis muscle through holes drilled in the distal end of the radius and the lunate bone. The result at the end of six months was good. Marti [558] reviews the entire subject of Madelung's deformity and concludes that the condition results from a combination of congenital predisposition, endocrine factors at puberty and repeated minor traumas. He feels that surgical intervention is seldom indicated and that progression of the lesion may be prevented by support.

Marottoli and Brocca [559] obtained stability and good range of motion in 1 case of traumatic dorsal subluxation of the distal end of the ulna

554. Etcheverry, A. J.: Study of Two Cases of Kienböck's Disease, Med. españ. **3**:220-226 (March) 1940.

555. Caby: Bilateral Cervical Rib with Osseous Rarefaction, and Kienböck's Disease of Both Arms, Mém. Acad. de chir. **66**:232-235 (Feb. 28-March 6) 1940.

556. Michaelis, L. S.: Locking Wrist, Lancet **2**:229-230 (Aug. 24) 1940.

557. Horwitz, M. T.: Anatomic and Roentgenologic Study of Wrist Joint: Observations on Case of Recurrent Radio-Carpal Dislocation Complicating Madelung's Deformity and Its Surgical Correction, Surgery **7**:773-783 (May) 1940.

558. Marti, T.: Madelung-Dupuytren's Disease with Report of Case, Rev. méd. de la Suisse Rom. **60**:31-50 (Jan. 25) 1940.

559. Marottoli, O. R., and Brocca, M.: Fibrocartilaginous Lesions of Inferior Radiocubital Joint, An. de cir. **6**:79-84 (March) 1940.

by extirpating the fibrocartilage, reconstructing the radioulnar ligament and encircling the ulna with stout linen.

Roentgen Examination of the Carpus.—Graziani [560] analyzes the routine roentgen examination of the carpus and points out that many important details are missed. He proposes modification of the technic and suggests sixteen possible views for the exhaustive study of the wrist. These comprise: a dorsopalmar view with the wrist straight and with the wrist in radial and in ulnar deviation; a palmodorsal view with the wrist in the same three positions; a radioulnar view with the wrist straight and with it in flexion and extension; an ulnoradial view with the wrist the same in three positions; two radioulnar oblique views and two ulnoradial oblique views. In particular these projections were effective as follows:

1. In both the dorsopalmar and the palmodorsal view with the hand in ulnar deviation there is shown a full profile of the scaphoid without overlapping of the carpal bones at the distal third.

2. In the palmodorsal view, superimposition of the capitate and hamate bones is avoided, and the articulations of the two bones are clearly shown.

3. In the palmodorsal position with ulnar deviation there is good visualization of the articulation between the hamate and the triquetrum bones and of the partial dissociation of the pisiform and triquetrum bones.

4. In the palmodorsal view an anteroposterior aspect of the styloid process of the ulna is shown; in the dorsopalmar view the profile is shown.

5. The best visualization of the pisiform bone is obtained in the ulnoradial view with the wrist straight.

6. The ulnoradial view with the hand flexed offers the best visualization of the scaphoid bone in the distal half and of the articulations of the scaphoid with the greater multangular bone.

7. With the hand in hyperextension, both the radioulnar and ulnoradial view show the articulation of the capitate and semilunar bones.

8. With the hand in hyperextension, the ulnoradial view shows well the greater and lesser multangular bones.

9. The best visualization of the greater and lesser multangular bones is obtained in the oblique dorsoradial view.

10. The oblique dorsoulnar view is best for an accurate profile of the carpal bones. [ED. NOTE: This is the routine view commonly employed for demonstrating fracture of the middle of the scaphoid bone which may not be visible in any other view.]

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560. Graziani, A.: Roentgenological Study of the Wrist, Radiol. med. **27:** 382-392 (May) 1940.

Anatomy of the Hand.—The detailed anatomy of the midpalmar compartment is thoroughly described by Anson and Ashley.[561] On the basis of numerous dissections they describe and beautifully illustrate the compartment with the associated spaces and limiting layers. They conclude that the thenar space of Kanavel "lies between the lateral septum and the adductor pollicis fascia." The midpalmar space "is merely a bilaminar arrangement, whereby the floor of the fascial lining of the midpalmar compartment is locally split over the region of the last three metacarpal bones." They summarize their findings by saying

> that the regular, simple stratification is altered—and rendered complex—in the hand by interposition of the long flexor tendons of anti-brachial origin; in producing a specialized sheath for these structures a bilaminar tube results, fastened by aponeurotic septa to skin and to bones, itself divides into compartments for its contents. Branches of arciform arteries, superficial and deep to the sheath, communicate through anastomotic stems which use the intravaginal septa as their means of transmission.

The clinical need for such anatomic knowledge in the treatment of infections is well illustrated by Pemberton.[562]

Dupuytren's Contracture.—Hancock[563] suggests that Dupuytren's contracture is not a definite entity but that the local manifestation of a metabolic disturbance, such as gout, rheumatism, focal infection or trauma, may be a contributing cause. Griswald, in discussing Hancock's paper, reports a case in which a nodule proved to be a neurofibroma and was removed from the palm of an otherwise normal hand; a typical Dupuytren contracture later developed.

Meyerding[564] cites examples from 315 patients with Dupuytren's contracture, of whom he operated on more than 100, to illustrate the advantage of complete excision of the palmar fascia followed by splinting and physical therapy. He noted the frequent occurrence in the early stages of local soreness or redness of the palm. A similar phenomenon has appeared postoperatively in the absence of infection. He believes that "repeated trauma may be a possible exciting factor in the causation of the contracture," but he suggests also "removal of foci of infection and improvement of the general health" in the interest of prevention of the disease. Variability in the rate of progress is remarkable. Meyerding records occasional arrest for years of the progress of the deformity.

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561. Anson, B. J., and Ashley, F. L.: Midpalmar Compartment, Associated Spaces and Limiting Layers, Anat. Rec. **78**:389-407 (Nov. 25) 1940.

562. Pemberton, P. A.: Infection of the Fascial Spaces of the Palm, Am. J. Surg. **50**:512-515 (Dec.) 1940.

563. Hancock, J. D.: Dupuytren's Contracture, Kentucky M. J. **38**:290-293 (July) 1940.

564. Meyerding, H. W.: Treatment of Dupuytren's Contracture, Am. J. Surg. **49**:94-103 (July) 1940.

König [565] agrees with the prevalent opinion that the lesion is caused by constitutional and hereditary factors. Pathologic studies show hyperplasia in the initial stage and contracture in a late stage.

Ferrarini [566] is unique among authors in debating the significance of the contracture as an occupational disease. He notes that there is no established precedent or even consideration of the problem in the Italian statutes, and he finds little help in the reports from other countries. He collects at great length and classifies all available opinions; his work represents a monumental task of combing the literature. However, he offers nothing new and concludes that while there is no proof of the causal relation of trauma, proof of a constitutional factor or individual predisposition is equally difficult from a legal or insurance standpoint.

Snapping Fingers.—From a study of 20 cases of congenital contracture of the thumb, Beck [567] concludes that the deformity is always tendinous. Dermatogenous and myogenous contractures are traumatic. In the 20 cases studied there were hard nodules in the tendons of the flexor muscles, but none of the thumbs snapped. In 1 there was an associated fourth finger that did. Pathologic changes consisted of a nodular enlargement of the tendon just proximal to a hard thickening of the sheath. When the sheath was only divided, the recovery was incomplete in most cases; but when the hard area was excised, the recovery was complete. The pathologic changes seemed to be degenerative. The author concludes that congenital contracture of the thumb is a hereditary deformity which is a recessive characteristic and more prevalent in women than in men. He advises operation because conservative treatment rarely gives satisfactory results. He cites Jahss [568] in support of this opinion. [ED. NOTE: In the article cited Jahss said, "There is only one treatment and that is surgical." In a personal communication to one of us (W. P. B.) he added that he had never tried conservative treatment. Jahss distinguishes between trigger finger and congenital contracture. Either condition is more distressing to the mother than it is to the child. Simple contracture will invariably yield to conservative treatment, such as splinting and gentle manipulation. In a series of 6 cases of trigger thumb in infants all the patients recovered completely after treatment by splinting. In 1 case there was recurrence after removal of the splint, but the patient recovered spontaneously with-

565. König, E.: Dupuytren's Contracture, Med. Klin. **36**:568-571 (May 24) 1940.

566. Ferrarini, M.: Dupuytren's Contracture Can Be Considered as Occupational Disease, Rassegna di med. indust. **11**:70-97 (Feb.) 1940.

567. Beck, W.: Congenital Contracture of the Thumb, Arch. f. orthop. u. Unfall-Chir. **40**:318-325, 1940.

568. Jahss, S. A.: Trigger Finger in Children, J. A. M. A. **107**:1463-1464 (Oct. 31) 1936.

out further treatment. There is no more justification for the operative treatment of this condition in an infant than there is for open reduction of a fracture of the distal end of the radius in a child.]

Schörcher [569] reports a case in which the patient was a 25 year old woman with traumatic rupture of the radial strand of the tendon of the flexor digitorum sublimis muscle; the lesion gave rise to a snapping finger of unusual origin. The enlargement of the tendon was found to snap at operation. Spisic [570] was impressed by the disability entailed by snapping of his own fifth finger. He had to undergo operative treatment before he could comfortably and efficiently continue his surgical practice.

Operations on the Fingers.—Burman [571] reports using a vitallium thimble in two arthroplasties on interphalangeal joints. The results were most encouraging.

Kaplan [572] suggests the need for operation to reduce the typical mallet or baseball finger. In his opinion the original deformity is frequently due to displacement of the joint rather than to avulsion of the attachment of the tendon. Usually the cause is a rupture of the tendon of the extensor muscle or a fracture of the base of the terminal phalanx. For rupture of the tendon, he urges operation; for fracture he feels that the results will be improved by open operation.

Jelsma [573] suggests the use of ordinary collodion to maintain extension of the distal interphalangeal joint of a finger. He severed the extensor tendon of his own index finger. After the wound had healed, he was able to operate when collodion was painted on the distal two phalanges with the distal joint in extension. He felt that the constricting effect of collodion was desirable.

Injury of the Digits.—Schoolfield [574] enters a plea for early recognition of and prompt attention to injuries of the first carpometacarpal joint with rupture or overstretching of the capsule but without injury to the bone. Dorsal dislocation of the base of the first metacarpal bone usually leads to relaxation of the capsule if immobilization with traction

569. Schörcher, F.: Snapping Finger Due to Injury to the Tendons, Zentralbl. f. Chir. **67**:627-628 (April 6) 1940.

570. Spisic, B.: The Trigger Finger, Zentralbl. f. Chir. **67**:157-159 (Jan. 27) 1940.

571. Burman, M. S.: Vitallium Cap Arthroplasty of Metacarpophalangeal and Interphalangeal Joints of Fingers, Bull. Hosp. Joint Dis. **1**:79-89 (Oct.) 1940.

572. Kaplan, E. B.: Mallet or Baseball Finger, Surgery **7**:784-791 (May) 1940.

573. Jelsma, F.: Finger Splint That Will Not Impair Hand Function, Am. J. Surg. **50**:571-572 (Dec.) 1940.

574. Schoolfield, B. L.: Injuries About Carpometacarpal Joint of Thumb, South. M. J. **33**:354-355 (April) 1940.

is not promptly applied. When the relaxation becomes chronic, the author suggests surgical closure of the tear and plication of the capsule. Nutter [575] emphasizes the need for traction and rotation to free the sesamoid bones and reduce them to their normal position when digital sesamoid bones are caught in a dislocation of the joint of a phalanx. He reports 2 cases, in one of which open reduction was necessary; in the other closed reduction was done by preliminary traction and rotation and then manipulation of the ends of the bones.

Williams [576] reports 3 cases in which hysteria was associated with marked edema in the hand and the forearm. The swelling was attributed to associated dependency and immobility. The edema disappeared with elevation. In 1 case there was permanent damage with extension contractures of the fingers after eighteen months of swelling. Three experiments were performed to show the effect of dependency and immobility on the hand. [ED. NOTE: There is no record of careful investigation to rule out self-imposed constriction near the elbow as a factor in the production of edema, although this was probably considered by the author.]

XIX. TECHNIC, AMPUTATIONS AND APPARATUS

New or Improved Operations.—Hatt [577] reports using for seven years a technic of central bone grafting for arthrodesis of the knee which has facilitated that none too easy procedure and has been associated with no unfortunate complications or retardation in growth, even though the tibial graft passes completely through both epiphysial lines adjacent to the joint. An analogous technic has also been used advantageously on the ankle. [ED. NOTE: The fact that retardation of growth has not occurred in these cases confirms the belief of one of us (J. W. W.) that curettage or cauterization of the metaphysial plate in using White's modification of Phemister's technic of epiphysiodesis is unnecessary.]

Encountering the usual difficulty in passing the long head of the biceps muscle through the bone tunnel in the Nicola operation, Baker [578] employs a piece of Dakin's tubing 3 mm. in its inside diameter, 1 mm. thick and 15 cm. long as a tendon carrier. The tubing, the opening of which has been dilated by a hemostat, is slipped over the end of the tendon after the stay suture in the proximal portion of the tendon has been passed through the tube. A silver wire hairpin is then passed

575. Nutter, P. D.: Interposition of Sesamoids in Metacarpophalangeal Dislocations, J. Bone & Joint Surg. **22**:730-734 (July) 1940.

576. Williams, C.: Hysterical Edema of Hand and Forearm, Ann. Surg. **111**: 1056-1064 (June) 1940.

577. Hatt, R. N.: Central Bone Graft in Joint Arthrodesis, J. Bone & Joint Surg. **22**:393-402 (April) 1940.

578. Baker, L. D.: Nicola Operation: Simplified Technique, J. Bone & Joint Surg. **22**:118-119 (Jan.) 1940.

through the bone tunnel, and the tubing is pulled through and is followed by the tendon. Baker values highly the soft, flexible silver wire loop which simplifies pulling the tubing and tendon through the tunnel. [ED. NOTE: One of us (J. W. W.) has simplified this technic by cutting a deep trench in the head, slipping the uncut tendon into it and replacing the excised piece.]

Harmon and Krigsten [579] discuss rather extensively the problem of legs of unequal length and report a somewhat limited experience with various corrective procedures. They mention that undercorrection rather than overcorrection has been the most frequent error. They mention the unsuitability of shortening the legs of children; to a lesser degree the same holds true for adults. On the other hand, they state that lengthening should be done only by experienced surgeons with adequate equipment and suitable surroundings. [ED. NOTE: This is an article well worth reading in full.]

Operations on Tendons.—Once more Bunnell [580] presents results of his wide experience with operations on tendons. He gives more rule of thumb advice, stating that primary repair of tendons should not be done except when the indications of time, condition of the wound, hospital facilities and special training of surgeons augur well. If conditions are not propitious, it is better to postpone repair of tendons until later and simply débride, close the wound loosely but securely and cover vulnerable parts. A delay of six months at least should be allowed if bone infection has complicated healing. If extensive operation is done at the time of the injury and sepsis follows, the subsequent procedures are much more difficult to perform and less likely to be successful. Performing repair of tendons when a sheath does not exist is most difficult and adds considerably to the probability of failure. Trauma must be reduced to a minimum, and a simple nonirritating stitch must be employed on the tendon. Bunnell recommends using a fine stainless steel wire and describes the manner of its insertion and removal. [ED. NOTE: This is another valuable contribution from a master surgeon in this field.]

Koch [581] in an article on the surgical principles of repair of divided nerves and tendons condemns the use of antiseptics in open wounds. He urges gentleness in handling the tissues and the use of soft sterile cotton and soapsuds for cleansing the wound instead of green soap and gauze. The soapsuds should be washed away with sterile water. This

579. Harmon, P. H., and Krigsten, W. M.: Surgical Treatment of Unequal Leg Length, Surg., Gynec. & Obst. **71**:482-490 (Oct.) 1940.

580. Bunnell, S.: Primary Repair of Severed Tendons: Use of Stainless Steel Wire, Am. J. Surg. **47**:502-516 (Feb.) 1940.

581. Koch, S. L.: Some Surgical Principles in Repair of Divided Nerves and Tendons, Quart. Bull. Northwestern Univ. M. School **14**:1-8, 1940.

should always be done with the patient under general anesthesia. The cuff of a sphygmomanometer should be used rather than an ordinary tourniquet. For the repair of tendons he recommends dry, unwaxed fine silk. The use of drains is discouraged. [ED. NOTE: This is a good article, well written and worthy of further study.]

Mason [582] describes the details of the technic of repairing tendons. He quotes Bunnell and joins with Koch in advising against the use of antiseptics. He, too, recommends soft cotton instead of gauze. Longitudinal incisions in the hand must be avoided whenever possible, because of the tendency of all scars to longitudinal contraction, particularly on the palmar surface. He also describes his favorite stitch for repairing tendons and advises making a window in the tendon sheath over a repair to avoid as much as possible the formation of adhesions. He is not so positive as Bunnell about the need of immediate repair.

New Surgical Instruments.—The continuance in popularity of the use of metals and alloys which resist corrosion and are nonirritating to tissue has resulted in the development of new surgical procedures. To facilitate the performance of these procedures, instruments are being devised which otherwise would never have been considered necessary.

The so-called vitallium cup arthroplasty of the hip of Smith-Petersen stimulated Norton [583] to devise an adjustable reamer for rounding the head of the femur to take the place of a battery of expensive handmade instruments. [ED. NOTE: One of us (J. W. W.) has watched Smith-Petersen use this instrument, and although the latter prefers the original solid cup-shaped reamers, he approves the adaptable reamer and recommends its use.] It has four adjustable cutting leaves which facilitate the actual procedure and reduce the time element in shaping the head. Because of difficulty in manufacture it is expensive; it is hoped that its cost can be reduced as it is made in larger quantities.

The return to greater popularity of internal fixation screws caused Tenopyr and Corriero [584] to devise what is erroneously called a jig for holding screws of various sizes together with their appropriate taps and drill points before their insertion into bone. With this holder one can see at a glance whether an adequate assortment of screws is available for an elected procedure. A new screwhead described by these authors differs from the usual slotted head; in a blank top surface a hexagonal hole has been made to receive a hexagonal wrench. The absence of the

582. Mason, M. L.: Primary and Secondary Tendon Suture: Discussion of Significance of Technique in Tendon Surgery, Surg., Gynec. & Obst. **70**:392-402 (Feb., no. 2A) 1940.

583. Norton, P. L.: Adjustable Reamer for Use in Arthroplasty of Hip, J. Bone & Joint Surg. **22**:458-459 (April) 1940.

584. Tenopyr, J., and Corriero, W. P.: Use of Tool Jig and New Type of Screw in Bone Plating, Am. J. Surg. **48**:475-476 (May) 1940.

slot helps to reduce the trauma associated with insertion of the screw, since slots tend to catch and tear soft tissue in the wounds. The use of the long hexagonal wrench, which fits snugly, facilitates insertion and largely eliminates the need for a screw-holding screw driver. Several improved designs of the latter have been put on the market but have not yet been described in the literature.

Surgeons who have had difficulty in securing adequate illumination of the interior of knees when performing arthrotomy will be glad to know of a self-illuminating retractor for the patella modeled by Cobey [585] after the Bennett steel retractor. Its chief handicap is that heat sterilization is not practicable for lucite, of which its retracting end is made, and cold chemical sterilization is required.

Best [586] describes an instrument devised to prevent a drill point from slipping off narrow rounded bones. [ED. NOTE: This appears to be a simple ingenious device, but one wonders whether there is any need for it. A sharp drill and an ordinary center punch usually suffice.]

Macey [587] has devised a new instrument for passing portions of tendon and fascia lata through long tunnels. It consists of a metal sleeve $\frac{3}{16}$ inch (0.48 cm.) in length. When it is forced down over a small pair of forceps, the teeth of which grip the end of a tendon, it holds the latter securely until it is released after being brought through the tunnel. [ED. NOTE: It seems that this would be more useful if it could be constructed so as to be flexible, particularly for work around the ankle.]

A distracting bone-holding apparatus somewhat on the order of the Anderson anatomic splint has been designed by Haboush,[588] who claims that better control of the fractured end of a bone can be obtained by two pins through both fragments, one pin being located near the fracture site. [ED. NOTE: The illustration of the apparatus gives the impression that it would be rather expensive, and one wonders whether the added risk of establishing direct communication into the fracture cavity with a pin so near it is justified by the questionable advantage of better control. It looks like a dangerous instrument in the hands of an inexperienced surgeon, and one feels that an experienced surgeon would devise some less hazardous method to accomplish his aims.]

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585. Cobey, M. C.: Self-Illuminating Patella Retractor, J. Bone & Joint Surg. **22**:1103 (Oct.) 1940.

586. Best, F.: New Instrument for Fixation of Drill, Zentralbl. f. Chir. **67**: 147 (Jan. 27) 1940.

587. Macey, H. B.: New Instrument for Passing Portions of Tendons and Fasciae Latae, Am. J. Surg. **47**:686 (March) 1940.

588. Haboush, E. J.: Principles Governing Treatment of Fractures and Bone Lengthening by Direct Skeletal Means and New Apparatus: Preliminary Report, Surgery **7**:356-363 (March) 1940.

For those surgeons who prefer the subcutaneous drilling of ununited fractures a guide has been devised by Shifrin [589] which permits the insertion of a drill into bone through a small ¼ inch (0.64 cm.) incision in the skin. It is large enough to take a 3/32 inch (0.24 cm.) drill point and has three sharp prongs beveled from the inside; it engages the bone and aids in getting the drill started. The instrument consists of a tempered steel tube 1½ inches (3.8 cm.) or more long, depending on the depth of the bone beneath the skin; a handle is attached to the tube at right angles. The guide can be easily directed so that holes may be drilled in any desired direction with great ease, since the bone is steadied by the prong-point guide.

Using the same principle employed in the White Smith-Petersen nail extension and extractor, Cahan [590] has devised a Moore-pin extractor which can be securely attached to the pin that is to be removed.

Overholt,[591] a thoracic surgeon, has devised a self-retaining scapula retractor, the idea of which might be employed in orthopedic operations in which surgical assistants are few or space for them at the operating table is lacking for one reason or another. The principle on which the apparatus depends is the employment of a rigid support entirely outside the operating field to which a sterile retractor, clamp or forceps might be attached, the latter being in the field of operation. One instance in which such a device might be of value is holding together tendons which are being united. [Ed. Note: Too many hands in a small field impede the operator, and yet in such instances traction in just the right place and in the required amount is most desirable. In this apparatus a reel and chain are the traction elements employed, but one of us (J. W. W.) suggests rubber bands as more adaptable and simpler.]

Metallic Internal Fixation.—Vitallium for internal fixation still seems to hold the stage, although a few authors have voiced the opinion that other alloys, particularly stainless steel, are practically as good and have the advantage of more strength. Among those who advocate the use of vitallium are Stuart,[592] Tuell,[593] Cameron [594] and Secord and

589. Shifrin, P. G.: Guide for Drilling Ununited Fractures, J. Bone & Joint Surg. **22**:1101-1102 (Oct.) 1940.

590. Cahan, A. M.: Cahan Nail Extractor, Am. J. Surg. **50**:140-141 (Oct.) 1940.

591. Overholt, R. H.: Self-Retaining Scapula Retractor, J. Thoracic Surg. **9**: 291-293 (Feb.) 1940.

592. Stuart, F. A.: Use of Vitallium Screws in Fractures of Long Bones, J. Oklahoma M. A. **33**:8-11 (May) 1940.

593. Tuell, J. I.: Vitallium in Internal Fixation in Bone Surgery, Northwest Med. **39**:163-165 (May) 1940.

594. Cameron, D. M.: Vitallium in Bone Surgery with Particular Reference to Its Clinical Irritability, Proc. Staff Meet., Mayo Clin. **15**:561-564 (Sept. 4) 1940.

Breck.[595] The latter, because of the difficulty of removal, recommend that all vitallium be left permanently in place, assuming its complete inertness. Burke [596] in comparing the corrosive effect of various metals in tissues urges the use of a rare metal, tantalum, claiming that it "is comparable to steel in its strength, toughness and workability." This metal is not an alloy, and its behavior, if pure, is thus more dependable. No idea as to its cost or source is given. [ED. NOTE: This metal is not yet available for general use.]

Hudack [597] recommends a high chromium, low nickel steel alloy when certain requirements are fulfilled; it should be polished and "passivated by immersion in 20 per cent nitric acid at 65 C. for a half hour to give, theoretically, a molecular chromic oxide coating." Detailed and complicated instruction is given on how to reduce further the electrolytic corrosive action. [ED. NOTE: The latter might tend to deter one from using this alloy if he did not appreciate that all material to be left in tissue should be more or less passivated.]

Bothe, Beaton and Davenport [598] report a series of experiments with animals in which various metals as well as two alloys were embedded in bone. It was found that pure manganese promoted the production of much callus and that titanium was as well tolerated as vitallium and stainless steel. [ED. NOTE: The formula is not given.] They are of the opinion that reaction of living tissue, particularly bone, is a chemical rather than an electric phenomenon. The physical properties of manganese do not permit its use as a metal. They call attention to the value of titanium, lamenting that metallurgists have not yet found a way to work it.

The use of the vitallium wood type screw instead of the Sherman type is advocated by Stuart.[592] However, only a small series of cases is reported. [ED. NOTE: The conclusions may be premature, at least about the design of the screws.] This author recommends the use of vitallium for internal fixation. [ED. NOTE: In the opinion of one of us (J. W. W.) the ideal material has not yet been found, and it is his belief that in the not too distant future, possibly as the result of efforts associated with the present war, a more satisfactory agent, whether pure

595. Second, E. W., and Breck, L. W.: Report of Case in Which Vitallium Plate Could Not Be Removed, J. Bone & Joint Surg. **22**:749 (July) 1940.

596. Burke, G. L.: Corrosion of Metals in Tissue and Introduction to Tantalum, Canad. M. A. J. **43**:125-128 (Aug.) 1940.

597. Hudack, S.: High Chromium: Low Nickel Steel in Operative Fixation of Fractures, Arch. Surg. **40**:867-884 (May) 1940.

598. Bothe, R. T.; Beaton, L. C., and Davenport, H. A.: Reaction of Bone to Multiple Metallic Implants, Surg., Gynec. & Obst. **71**:598-602 (Nov.) 1940.

metal or alloy, will be discovered. It is becoming more evident that while vitallium appears to be the most inert material its brittleness and lack of strength in general subtract from its usefulness to a considerable extent. When strong internal fixation material is needed the better type of stainless steel seems to be most popular, that is, the so-called 18 to 8 alloy.]

Amputations.—The Council on Physical Therapy of the American Medical Association published three chapters of a proposed Handbook on Amputations in the latter part of 1940, all of which were written for and are helpful to the occasional amputator, as most surgeons fortunately are. The first chapter,[599] which treats of psychologic and physiologic principles in amputations, is the least practical; the use of cineplastic technic is discouraged because it depends for its success on too many uncertain and difficult factors, not the least important of which is the manufacture of the prosthesis itself.

The second chapter,[600] which is devoted to general principles, is most valuable but emphasizes points perhaps of questionable value, such as preparing the end of the bone for weight bearing. For this it is recommended that periosteum be removed for a distance of an inch (2.5 cm.) from the bone ends to prevent abnormal formation of the bone. This is at variance with Verrall's ideas.[601] He is a prominent English surgeon who has had much experience with amputations and who claims that special care of the periosteum is necessary. He states that injection of alcohol into the nerves causes alcoholic neuritis and should therefore be abandoned. He believes that terminal neuroma cannot be avoided. The end of the nerve should be placed where it is most protected, and crushing the nerve should be avoided. He goes on to state that adequate hemostasis should be employed rather than drainage.

In the Council's chapter on general principles it is stated that disarticulations, particularly of the knee, should give physiologically the best stumps. Cooperation of the limb makers is difficult to get.

Rogers[602] writes a strong paper on the superiority of the weight-bearing amputation through the knee joint, giving as advantages: The weight-bearing surface is large; all tissues in the vicinity are adapted

599. Amputation: Psychologic and Physiologic Principles in Amputations, report of the Council on Physical Therapy, J. A. M. A. **115**:1719-1720 (Nov. 16) 1940.

600. Amputation: General Principles Governing All Amputations, report of the Council on Physical Therapy, J. A. M. A. **115**:1799-1801 (Nov. 23) 1940.

601. Verrall, P. J.: Amputation Stumps and Artificial Limbs, Brit. M. J. **1**: 62-64 (Jan. 13) 1940.

602. Rogers, S. P.: Amputation Through Knee Joint, Physiologic Amputation, Mississippi Valley M. J. **62**:174-176 (Sept.) 1940.

to weight bearing; there is no tension on parts; control of the quadriceps femoris and hamstring muscles is maintained; long leverage for control of the hip is provided; good control of rotation is had because of the shape of the end; the bulbous end permits lifting of the prosthesis without a belt; there is minimum atrophy of the muscles of the thigh; good vascularity is assured; the distal femoral epiphysis is preserved in growing children.

In the Council's third chapter [603] on amputations, sites are discussed. All amputations of the lower part of the leg through sites short of the toe and the anterior metatarsal bones is discouraged, except through the midtibia or higher if necessary, but not nearer than 2½ inches (6.4 cm.) of the knee. Most amputations below the middle of the tibia necessitate amputations later because of circulatory difficulties. It is important to leave at least the head of the fibula, to permit easier rotation of the prosthesis. The value of amputation through the thigh in the prone position is explained; it facilitates exposure of the vessels and allows better tailoring of the flaps. Rees [604] also advocates the prone position for amputations through the lower third of the femur, calling attention in addition to the points already noted, to the importance of suturing the tendons of the quadriceps muscles to those of the hamstring muscles, of using a single silk suture and also of keeping away from muscle tissue, especially when infection is possible.

In an effort to prevent all too frequent instances of embolism after amputation of a lower extremity Veal [605] urges the high ligation of the femoral vein as a preliminary measure. An excellent diagram accompanies the article and indicates plainly how much venous surface with its entering veins is eliminated by this procedure without disturbing the circulation in the stump.

Hebb [606] discusses amputation in light of his extensive experience in the World War. He states the ideal stump above the knee is 10 to 12 inches (25 to 30 cm.) long from the tip of the great trochanter with a posterior transverse scar 1½ inches (3.8 cm.) above the end. The ideal stump below the knee is 6 inches (15 cm.) of tibia with the fibula 1 inch (2.5 cm.) shorter. Above the elbow the most satisfactory stump is 8 inches (20 cm.) from the tip of the acromion process; bone

603. Amputation: Sites of Election for Amputation, report of the Council on Physical Therapy, J. A. M. A. **115**:2174-2176 (Dec. 21) 1940.

604. Rees, C. E.: Amputation Through Lower Third of Femur: Modified Technique, California & West. Med. **53**:64-66 (Aug.) 1940.

605. Veal, J. R.: High Ligation of Femoral Vein in Amputations of Lower Extremities: Preliminary Report Based on Twenty-Eight Amputations of Thigh, J. A. M. A. **114**:1616-1619 (April 27) 1940.

606. Hebb, J. H.: Amputation Sites and After Treatment, J. Roy. Nav. M. Serv. **26**:144-147 (April) 1940.

should not be sectioned less than 3 inches (7.5 cm.) above the elbow. In the forearm a stump 7 to 8 inches (18 to 20 cm.) from the tip of the olecranon process is desirable. One as short as 3½ inches (9 cm.) is of great value from the limb-fitting point of view. The importance of the elastic bandage dressing during convalescence is emphasized. [ED. NOTE: This is an excellent article giving the conclusion of a surgeon with a tremendous amount of experience.]

Contrary to the usual opinion of surgeons with wide experience with amputation, Guth,[607] a surgeon at present with the German army, cites his own Pirogoff amputation as advantageous. The amputation was done twenty years ago. He has carried on an extensive country practice and once won second prize in a skiing competition. [ED. NOTE: It is felt, however, that the few successful results after a Pirogoff amputation are the exception rather than the rule.]

A note of warning is sounded by Leclerc[608] urging patience in the surgical treatment of painful stumps, a large proportion of which he states improve spontaneously in the course of time. In cases in which the pain persists, particularly when the local injection of procaine hydrochloride gives temporary relief, lumbar sympathectomy or excision of the stellate ganglion in the upper extremity before nerve resection is performed is recommended.

Williams and O'Kane[609] suggest a guide for operation and the level of amputation in lesions of the lower extremities associated with diabetes. The two major elements of the lesions are arterial insufficiency and infection. Often, if the question of blood supply is not carefully considered, the distressing appearance of septic forefoot in a patient with diabetes will unduly influence even an experienced surgeon to resort to amputation as the safest course. Instrumental observations the authors do not feel are necessary for a correct chemical evaluation of arterial insufficiency. [ED. NOTE: The article is well illustrated and deserves thorough reading. Their table of diagnostic criteria is well worth studying. The timely attention directed to this matter will result in the saving of many limbs which otherwise might have been unnecessarily amputated.]

Haddan,[610] who is president of the Association of Limb Manufacturers of America, Inc., declares Lisfranc, Chopart and Pirogoff

607. Guth, K.: Pirogoff Method of Foot Amputation, München. med. Wchnschr. **87**:502-503 (May 10) 1940.

608. Leclerc, E. P.: Treatment of Painful Amputation Stumps, Presse méd. **48**:667-669 (Aug. 21-24) 1940.

609. Williams, F. W., and O'Kane, T. J.: Clinical Classification of Lesions of Lower Extremities Associated with Diabetes: Guide for Operation and Level of Amputation, Arch. Surg. **40**:685-693 (April) 1940.

610. Haddan, C. C.: Amputations to Obtain Greatest Functional Value, Rocky Mountain M. J. **37**:440-446 (June) 1940.

stumps are unsatisfactory and that Syme stumps are inferior to amputations done below the knee. He recommends a 7 inch (17.8 cm.) tibia to be ideal for the lower part of the leg with the fibula 2 inches (5 cm.) shorter. A minimum stump he states is 1½ inches (3.8 cm.) of the tibia, and in such cases the fibula should be removed. He condemns disarticulations through the knee joint and states that they are less efficient than Gritti stumps.

Close cooperation between the limb fitter and the surgeon is urged by Barling.[611] He mentions the "sentimental appeal" of the Syme amputation, stating that it is particularly applicable to children. He emphasizes extreme conservatism in amputation of the upper extremities.

The technic of a shoulder girdle amputation is described in detail by Haggart,[612] who states that the relatively simple method of identification and treatment of the subclavian vessels and brachial plexus is most effective. [Ed. Note: The technic is a modification of that described by Littlewood[613] in 1922. Haggart's article is most important to remember when need arises for this rare but occasionally necessary operation.]

Artificial Legs and Arms.—Jordan[614] calls attention to a newly devised ischial strap seat which is claimed to be much more efficacious than the simple Thomas ring. It transfers the body weight from the tuberosity of the ischium to the lateral upright longitudinal bar of a double bar leg brace. It is also claimed that it is easier to construct than one with the direct ischial support. [Ed. Note: This should be quite satisfactory if properly fitted.]

Dubois[615] states that an immediate or temporary prosthesis is of little value and urges the early use of a permanent apparatus. [Ed. Note: Probably most surgeons favor the permanent apparatus except when emergencies such as arise from war conditions occur or when the economic factor must be considered. For children, for instance, one of us (J. W. W.) is of the opinion that a temporary prosthesis is of definite value. Most government rehabilitation authorities rule that a patient must have reached his full growth before he is allowed a permanent limb paid for by public funds.]

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611. Barling, S.: Amputation of Extremities in Cases of War Wounds, Post-Grad. M. J. **16**:162-167 (May) 1940.

612. Haggart, G. E.: Technic of Interscapulothoracic Amputation, Lahey Clin. Bull. **2**:16-22 (July) 1940.

613. Littlewood, H.: Amputations at Shoulder and at the Hip, Brit. M. J. **1**: 381-383 (March 11) 1922.

614. Jordan, H. H.: New Ischial Seat Brace for Elimination of Weight Bearing, J. Bone & Joint Surg. **22**:1097-1100 (Oct.) 1940.

615. Dubois, M.: The Amputation of the Lower Extremities, Helvet. med. acta **6**:781-817 (March) 1940.

Braces.—Appreciating the actual danger of further damage to the spinal cord during the application of adequate support in the form of a plaster of paris cast to patients with injuries in the cervical portion of the spine and neurologic symptoms, Wegner and Munro[616] have attached for the purpose of immobilization a conventional back brace to the posterior lower part of a turnbuckle cervical extension brace. The importance of hyperextension, even during late convalescence, is emphasized. [ED. NOTE: This brace has been used in only 2 cases, and on looking at the illustrations one wonders if the addition of the spinal part is essential, except for injuries in the lower cervical or the upper dorsal region of the spine. If the usual hyperextension of the spine is obtained by the ordinary turnbuckle cervical brace with adequately placed generous anterior and posterior supports, one of us (J. W. W.) cannot see the necessity of extension of the spine save for fractures in the lowest cervical and the upper dorsal region of the spine. However, these are held satisfactorily by the Calot jacket.]

For fractured ribs and other injuries in the wall of the chest Steven[617] has devised a wide belt or binder in which there is an elastic element to allow expansion of the well side, the rest of it being nonelastic. It is claimed to give satisfactory immobilization on the side affected.

A rather complicated ambulance stretcher has been designed by Morrison.[618] It incorporates the idea of a hyperextension spinal frame for the safer transportation of persons with injuries of the back. There is an intrinsic spring traction arrangement for both the upper and the lower extremities. A central vertically placed padded board extending up to the perineum for temporary counter traction is a part of the equipment. [ED. NOTE: Since actual harm is done relatively frequently to patients with injuries of the spine by inexperienced ambulance drivers, the appearance of this apparatus, which should not be too expensive to manufacture, is welcomed, particularly as it is arranged so as to allow some degree of head traction. An added advantage is that roentgenograms of any part of the body, at least in one direction, can be taken without disturbing the patient.]

A restraint apparatus of simple and apparently efficient design has been described by Kaplan, Levinson and Lewin.[619] It consists of three 6 inch (15 cm.) unbleached muslin bands which are strapped around a

616. Wegner, W., and Munro, D.: Cervical-Spine Brace Which Reduces Use of Plaster Casts, New England J. Med. **223**:458-460 (Sept. 19) 1940.

617. Steven, R. A.: New Type of Belt for Splinting Chest, California & West. Med. **53**:84-85 (Aug.) 1940.

618. Morrison, G. M.: Stretcher Splint for Safely Transporting the Injured, Am. J. Surg. **48**:700-702 (June) 1940.

619. Kaplan, M.; Levinson, S. O., and Lewin, P.: Simple, Effective, Fabric Restraint-Splint, J. A. M. A. **115**:1098-1099 (Sept. 28) 1940.

mattress at suitable levels, so that other 2 inch (5 cm.) bands can be stitched to them; these buckle around both extremities just above the ankle, the knee and the wrist. Another wide muslin band passes around the foot of the bed; to this are fastened two other 2 inch (5 cm.) bands which hold the forefoot securely in place preventing drop foot and rotation at the same time. If necessary, it is thought that other bands might be used around the chest, the head and the pelvis for further immobilization of an intractable patient, holding him down in Gulliver fashion without risk of injury.

Dubs [620] tells of a quickly adjustable temporary splint for transportation; it is for both the upper and the lower extremities, different countertraction crutches being used for the arms and for the legs. The apparatus is original in that a single four-edged bar is used to which the various attachments for traction and countertraction are applied. Its chief advantages are its ease of application and the fact that it can be applied over clothing.

A modification of the Böhler abduction shoulder brace is presented by Parsons and Hart.[621] It does not extend down over the iliac crest on the affected side. It is claimed that this extension down over the crest is not necessary and that if it extends down just a little below the costal border it is just as efficient and allows the patient much more freedom. [ED. NOTE: This departs considerably from the usual custom in all abduction braces and should be thoroughly tried out before being accepted.] They also recommend that plaster shoulder spicas should never be applied with the patient under anesthesia. [ED. NOTE: One of us (J. W. W.) does this as a routine.]

Hundemer [622] describes a Cramer or Böhler support which with stability allows the turning of the upper arm as well as movements in vertical and horizontal directions. [ED. NOTE: If the device permits all this flexibility, it is difficult to understand how it can be stable.]

Traction Apparatus.—Baker and Hawkes [623] describe an apparently easily assembled trapezoidal apparatus hinged at its four corners and controlled with an internal diagonal turnbuckle which serves as the basis of the traction arrangement in which the well leg is used to fix and reduce the injured leg, the pelvis serving as a fulcrum. The apparatus is clamped onto the casts regularly applied in this method of treatment,

620. Dubs, J.: New Extension and Fixation Splint for Arm for Transportation Purposes, Schweiz. med. Wchnschr. **70**:193-195 (March 2) 1940.

621. Parsons, K. O., and Hart, A. T.: Splinting Fractures of Humerus, Brit. M. J. **1**:726-728 (May 4) 1940.

622. Hundemer, W.: Adjustable Arm Splint Permitting Turning of Upper Arm, München. med. Wchnschr. **87**:568-569 (May 24) 1940.

623. Baker, M., and Hawkes, S. Z.: New Apparatus for Well Leg Traction, Am. J. Surg. **49**:523-525 (Sept.) 1940.

and the push-pull action is instituted with the turnbuckle as desired. The authors briefly discuss the type of injuries for which the apparatus is adapted, stating justifiably that it is best suited for the intertrochanteric fracture. [ED. NOTE: In the illustration accompanying the article the leg casts seem unusually short. To be truly effective and immobilize the knees satisfactorily, they should go up further toward the groin than pictured. Unfortunately nothing is mentioned about transfixing plaster-incorporated pins. It is to be feared that if this device is employed by an inexperienced surgeon and any real degree of traction is applied, distressing sloughs will result.]

Overton [624] advocates the use of a simple foot plate combined with a spreader for use in traction of the skin on the lower extremity. In order to prevent drop foot, traction is applied to a cross bar on the gutter foot piece posterior to or below the spreader about an inch (2.5 cm.). [ED. NOTE: This simple apparatus might be of more value if to prevent rotation of the leg one of the cross bars could be extended a few inches on either side and bent down to rest on the surface of the bed.]

The value of intrinsic elastic band traction replacing weight and pulley equipment is advocated by McKinnon.[625] He sets forth its advantages in a most convincing manner. In order to know just how much traction is being applied he suggests that a small 25 pound (11.3 Kg.) spring balance be hooked up in series with the rubber bands. [ED. NOTE: This method has been used for years by one of us (J. W. W.) with complete satisfaction. A spring balance manufactured by Chatillon is most satisfactory.]

Rogge [626] describes a sliding splint for immobilization and extension at the front of fractured legs. The splint is said to have been valuable during the World War. [ED. NOTE: From the description, the arrangement appears to be too simple to be efficient, and it is to be feared that except for emergencies such as occur in military engagements it would be impracticable.]

Skeletal cranial traction for fractures and dislocations in the cervical region of the spine is recommended by Zorn,[627] who uses a wire loop beneath the outer table of the skull. [ED. NOTE: The apparatus he

624. Overton, L. M.: Simple Foot Plate for Use in Skin Traction on Lower Extremities, J. Iowa M. Soc. **30**:110 (March) 1940.

625. McKinnon, S. D.: Fractures—Elastic Band Traction, Canad. M. A. J. **43**:324-327 (Oct.) 1940.

626. Rogge, H.: Sliding-Splint Bandage for Splinting and Nonsurgical Extension of Leg Fractures at Front, München. med. Wchnschr. **87**:281-284 (March 15) 1940.

627. Zorn, L.: Cranial Wire Extension in Fractures of Cervical Vertebrae, Zentralbl. f. Chir. **67**:850-852 (May 11) 1940.

describes does not appear to be nearly so efficient nor so easy to apply as those used in this country.]

Another orthopedic table is described by Saigo.[628] In it the arrangement for vertebral traction, especially in the cervical region, has been emphasized. [ED. NOTE: Skeletal traction is not mentioned, and it is doubtful whether any new principles have been employed.]

Plaster Cast Technic.—The advantages of plaster of paris bandages prepared in a hospital are taken up by McLin [629] in a well written article. The capacity of satisfying the desires of individual surgeons as well as saving money is stressed. He urges the employment of periodic setting time tests and calls attention to the importance of having a dry storage place.

Girdlestone [630] describes the cream-fabric method advocated by Trueta for rapid application of the plaster cast. Excellent pen and ink illustrations accompany the article. He also gives rather implicit directions to the beginner in the plaster technic.

Recognizing the difficulty of removing plaster casts, particularly skin plaster, Bickford [631] has devised an ingenious can opener method. The cast is cut by winding up on a heavy hemostat a section of piano wire, placed under the cast when it was applied. For casts more than ½ inch (1.3 cm.) thick, he doubles the wire back on itself as many times as needed. No. 22 (English gage) wire is the heaviest piano wire that can be satisfactorily wound up on a hemostat, and any size smaller than no. 26 is too weak. [ED. NOTE: It sounds simpler and more practical than some other methods which use a somewhat similar principle. It is worth trying.]

Cogswell and Thomas,[632] in discussing windowed casts, advise that the window be cut when the plaster is fresh and the edges beveled so that the part nearest the skin is larger than the external opening. This will prevent the distressing bulging of edematous tissue through the aperture, and the necessary amount of skin pressure over the wound can be more easily maintained. [ED. NOTE: Waterproofing the plaster plug will probably cause too much sweating to be satisfactory unless the dressings are frequent or unless the window is small.]

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628. Saigo, V.: Mechanism of Vertebral Fractures, Orthopedic Table for Reduction and Fixation, Zentralbl. f. Chir. **67**:106-110 (Jan. 20) 1940.

629. McLin, W. C.: Hospital-Made Plaster Bandages, Mod. Hosp. **55**:51-53 (Aug.) 1940.

630. Girdlestone, G. R.: Plaster-of-Paris, Lancet **2**:287-291 (Sept. 7) 1940.

631. Bickford, R. G.: Rapid and Painless Method of Removing Plaster Casts, Brit. M. J. **1**:539-540 (March 30) 1940.

632. Cogswell, H. D., and Thomas, C. A.: Method for Protecting Skin in "Windowed" Unpadded Casts, Am. J. Surg. **49**:409-410 (Sept.) 1940.

The Trueta treatment of war wounds with plaster casts is reported favorably by Ricard, Francillon, Deplante and Mathevon.[633] They emphasize the importance of having experienced men to apply the cast, as success depends largely on the manner of application. They urge delay in extracting projected fragments of bone and warn about the high incidence of ankylosis in patients with injured joints.

To hold bivalve casts neatly and accurately together, Rounds [634] recommends a folded-over strip of hard coated rapid-drying plaster to which nickle-plated boot hooks have been riveted at the edges of the plaster halves. [ED. NOTE: As they seem to be fastened to the cast only by the cementing property of the plaster strips, one wonders how well they will stay in place if any real tension is placed on them. The need for such an arrangement is admitted to replace unsightly adhesive straps, and it is hoped that this suggestion will prove practicable.]

To replace clumsy and noisy walking irons, injurious to furniture and flooring, Stryker [635] recommends that rubber heels be incorporated in the sole of the plaster casts where weight bearing is desired.

As a substitute for a steel and leather back brace, Mitchner [636] describes a suspender-like arrangement made of plaster reenforcements which he claims is efficient. For particularly heavy people he reenforces the strips which are well padded underneath with molded duralumin or tin. [ED. NOTE: The idea hardly seems practicable but may be worth a trial by the plaster enthusiast.]

Roentgen Technic.—In a reassuring article Garland and Morrissey [637] state that although iodized poppyseed oil (30 to 60 per cent) enters the cranium in two thirds of the cases in which it is used as a diagnostic aid in the spinal canal, it causes no trouble. What symptoms exist may be definitely attributed to causes other than the presence of the oil. [ED. NOTE: This is not the general belief about iodized poppyseed oil. Physicians are still awaiting the discovery of an absorbable opaque substance for this work, regardless of optimistic opinions about the presence of the oil to the contrary.]

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633. Ricard, Francillon, Deplante and Mathevon: Therapy of Extensive Traumatisms of Extremities by Plaster Cast and Rare Dressings: Study Based on Experience in Spanish War, Lyon chir. **36**:573-583, 1940.

634. Rounds, R. C.: Method of Maintaining Cut Edges of Split and Bivalved Casts in Accurate Apposition, J. Bone & Joint Surg. **22**:1088-1089 (Oct.) 1940.

635. Stryker, H. H.: Rubber Heels for Walking Casts, Surg., Gynec. & Obst. **70**:841-842 (April) 1940.

636. Mitchner, J. M.: Double-Bar Plaster Black Support, J. Bone & Joint Surg. **22**:456-457 (April) 1940.

637. Garland, L. H., and Morrissey, E. J.: Intracranial Collections of Iodized Oil Following Lumbar Myelography, Surg., Gynec. & Obst. **70**:196-210 (Feb.) 1940.

A rather complicated arrangement for making accurate roentgenograms of the neck of the femur is reported by McKenna.[638] A shockproof x-ray unit is placed beside a radiolucent perineal post measuring 4 inches (10 cm.). A plate holder is placed over the lateral aspect of the hip. The technic is further complicated by the suggestion that two portable x-ray units be used. [ED. NOTE: It is the opinion of one of us (J. W. W.) that a lateral view obtained by flexing and rotating the hip is far easier to procure, particularly if the patient can be placed on a genitourinary x-ray table with a Bucky diaphragm and a stationary tube. A technic of this type has been used by one of us (J. W. W.) for years with complete satisfaction, and he feels that taking lateral views in the horizontal plane of the table is not necessary.]

An important discussion of errors in the interpretation of roentgenograms has been published by Goldhamer and Swanberg.[639] [ED. NOTE: One point was not mentioned which most orthopedic surgeons consider important, namely, that every roentgenogram should be seen and interpreted by the surgeon ordering it as well as by the roentgenologist. In taking certain roentgenograms it is most important to have the surgeon either present or know exactly how it is taken.] The authors correctly emphasize the importance of knowing just where the central ray passes through the part shown in the roentgenogram. [ED. NOTE: One of us (J. W. W.) believes it would be most desirable to have some way of recording the location of this central ray on the film.]

White [640] has evolved a relatively simple method of graphically recording the discrepancy of legs of different length. The discrepancy is measured by the vertical difference between the horizontal lines drawn tangent to the top of the heads of the femurs on a roentgenogram of the pelvis taken while the patient is pushing both feet against a horizontal foot board on the usual Bucky x-ray table. He admits that there is a small distortion with this method, but since the same factor persists throughout other measurements in the same case, it tends to cancel itself out as an error. He has found this method most satisfactory and far more accurate than the bony landmark–tape line measurement.

Miscellaneous.—Albee [641] describes a new type of fracture table designed to facilitate extensive roentgen examinations and yet sacrifice

638. McKenna, H.: Device for Making Accurate Roentgenograms of Neck of Femur During Reduction, Surg., Gynec. & Obst. **71**:808-810 (Dec.) 1940.

639. Goldhamer, K., and Swanberg, H.: Errors in Roentgen Interpretation, Mississippi Valley M. J. **62**:136-142 (July) 1940.

640. White, J. W.: Practical Graphic Method of Recording Leg Length Discrepancies, South. M. J. **33**:946-949 (Sept.) 1940.

641. Albee, F. H.: Albee-Comper Fracture Table, Am. J. Surg. **47**:160-166 (Jan.) 1940.

none of the advantages of the most up-to-date operating table. Many new improvements are claimed for it, especially in regard to the care of injuries to the spine.

Santy and de Williencourt [642] have devised an apparatus which they state can be attached to any operating table for the purpose of holding the patient in a position of ventral decubitus during the application of a plaster cast employed in the treatment of conditions involving the spinal column. [ED. NOTE: While the apparatus appears ingenious, it does not appear to be practical for all types of cases.]

XX. RESEARCH

Vitamins.—Wille [643] uses a preparation containing water-soluble vitamin C and B_1 in their natural forms in the treatment of arthritis, particularly arthritis deformans in elderly women. The aim of his report is to prompt physicians to make further use of water-soluble vitamins in treating arthritic conditions. He prefers that the vitamins be given in their natural form, despite the fact that the exact nature of their action has not been established.

Liu [644] states that the fundamental defect involved in osteomalacia is an altered state of the intestinal tract on account of which calcium is either not absorbed or absorbed with difficulty. Administration of vitamin D will aid the absorption of calcium from the intestinal tract, but in addition a diet high in calcium should be given. Vitamin D when taken in large doses will be stored in the body if not used, and this supply will then be drawn on as needed to maintain a normal calcium balance.

Spies [645] states that vitamin B_6 (pyridoxine) at times has a dramatic beneficial effect in relieving muscular weakness and rigidity. It also lessens the rigidity in some cases of paralysis agitans. The symptoms of deficiency of vitamin B_6 may be adequately treated by intravenous injection of 50 mg. of this vitamin in physiologic solution of sodium chloride. Considerable improvement has been seen after its use in cases of pseudo hypertrophic muscular dystrophy.

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642. Santy and de Williencourt: Apparatus for Application of Plaster Cast in Ventral Decubitus in Spinal Disturbances, Lyon chir. **36**:614-617, 1940.

643. Wille, E.: Vitamins C and B_1 in Articular Rheumatism, Fortschr. d. Therap. **16**:118-122 (April) 1940.

644. Liu, S. H.: Role of Vitamin D in Calcium Metabolism in Osteomalacia, Chinese M. J. **57**:101-118 (Feb.) 1940.

645. Spies, T. D.; Hightower, D. P., and Hubbard, L. H.: Some Recent Advances in Vitamin Therapy, J. A. M. A. **115**:292-297 (July 27) 1940.

Stone [646] writes that vitamin E (given in the form of wheat germ oil) produces definite improvement in cases of muscular dystrophy; the addition of the vitamin B complex increases its efficacy.

Steinberg [647] reports that for muscular dystrophy one may give 2 cc. each day of wheat germ oil mixed with the vitamin B complex and that this promptly results in increased resistance to fatigue, in improvement of appetite and in normal muscles replacing rubbery muscles. For long-standing muscular dystrophy with contracture deformities, the administration of 4 to 6 cc. per day of wheat germ oil is suggested; no unpleasant after-effects have been noted. This dosage is also of value in the treatment of primary (but not of secondary) fibrositis.

In 1937 Mouriquand, Dauvergne, Tête and Edel [648] showed that by administration over a long period of a diet low in vitamin C it is possible to produce a syndrome of chronic ankylosing rheumatism with osseous decalcification in the epiphysis and metaphysis and osseous production at the periphery. They found that neither a scorbutigenic diet alone nor a scorbutigenic diet to which a small amount of vitamin C had been added would produce this syndrome. However, they now find that if small amounts of vitamin C and lemon juice are added to the scorbutigenic diet these changes are produced. They have not yet determined precisely which factors in lemon juice produce the osteophytic change but are continuing their experiments. They conclude that this osteophytic change like ordinary periosteoses is resistant to large doses of vitamin C, is irreversible and belongs to the group of paravitaminoses.

Steinberg [649] reports 30 cases of primary fibrositis treated by wheat germ oil in doses of 2 to 8 cc. daily for two to four months. Eight patients showed definite improvement in muscular soreness and stiffness; 12 had no relief.

Endocrine Secretions and Their Relation to Growth and Development of Bone.—Johnston [650] states that sexual maturation in the normal

646. Stone, S.: Treatment of Muscular Dystrophies and Allied Conditions: Preliminary Report on Use of Vitamin E (Wheat Germ Oil), J. A. M. A. **114**: 2187-2191 (June 1) 1940.

647. Steinberg, C. L.: Vitamin E in Treatment of Fibrositis, Am. J. M. Sc. **201**:347-459 (March) 1941.

648. Mouriquand, G.; Dauvergne, M.; Tête, H., and Edel, V.: Osteophytes Due to Chronic Avitaminosis, Compt. rend. Acad. d. sc. **210**:515-516 (April) 1940.

649. Steinberg, C. L.: Vitamin E in Treatment of Fibrositis, Am. J. M. Sc. **201**:347-349 (March) 1941.

650. Johnston, J. A.: Factors Influencing Retention of Nitrogen and Calcium in Period of Growth: Puberty in the Normal Girl and in the Girl with the Minimal Reinfection Type of Tuberculosis, Am. J. Dis. Child. **59**:287-309 (Feb.) 1940.

girl is accompanied by depression in the retention of calcium and nitrogen. This may precede or follow the menarche by several months, since the menarche is just one incident in this phase of growth. A physiologic rise and fall in the basal metabolic rate also occurs during puberty, and there is a direct parallelism between the retention of calcium and nitrogen and the basal metabolic rate. Evidence is presented which suggests that this phenomenon of decreased retention of calcium and nitrogen may be a contributing factor in the increased incidence of the reinfection type of tuberculosis in girls of this age group.

Avery, Scott and Conrad [651] found appreciable rise in blood calcium when chickens were given injections of estrone (theelin). When the administration of estrone was discontinued, the blood calcium came down to that of the control animals.

Ely and Phillips [652] injected estradiol benzoate into immature female rats in sufficient quantity to produce marked effects on uteri and ovaries but observed no demonstrable effects on the skeletal development. This does not confirm the results of the experiments of Gardner and Pfeiffer,[653] who report that estradiol benzoate causes the marrow cavities of female mice to be replaced almost completely by bone.

Sutro [654] concludes that injection of estradiol benzoate into immature female and male mice in various doses stimulates the proliferation of new bone in the medullary cavities of certain bones and especially in those of the lower end of the femur and the upper end of the tibia. The proliferation begins around the zone of provisional ossification and advances into the diaphysial portion of the bone. There is no increase in periosteal activity.

Wentworth, Smith and Gardner [655] injected estradiol benzoate into mice and report that it produces significantly higher concentrations of inorganic substances in the femurs and in the pelvis of mice receiving this substance than in control mice or in mice receiving testosterone propionate or estradiol benzoate plus testosterone propionate.

Rubinstein and Solomon [656] injected testosterone propionate intraperitoneally into male albino rats, beginning at the age of 26 days with

651. Avery, T. B.; Scott, H. M., and Conrad, R. M.: Blood Calcium Levels of Fowl Following Injections of Theelin, Endocrinology **27**:83-86 (July) 1940.

652. Ely, J. O., and Phillips, R. L.: Effect of Alpha Estradiol Benzoate on Skeletal Development of Immature Rats, Endocrinology **27**:661-663 (Oct.) 1940.

653. Gardner, W. U., and Pfeiffer, C.: Skeletal Changes in Mice Receiving Estrogens, Proc. Soc. Exper. Biol. & Med. **37**:678-679 (Jan.) 1938.

654. Sutro, C. J.: Effects of Subcutaneous Injection of Estrogen upon Skeleton in Immature Mice, Proc. Soc. Exper. Biol. & Med. **44**:151-154 (May) 1940.

655. Wentworth, J. H.; Smith, P. K., and Gardner, W. U.: Composition of Bones of Mice Receiving Estrogens and Androgens, Endocrinology **26**:61-67 (Jan.) 1940.

656. Rubinstein, H. S., and Solomon, M. L.: Growth-Stimulating Effect of Testosterone Propionate, Proc. Soc. Exper. Biol. & Med. **44**:442-443 (June) 1940.

doses of 0.05 mg. daily and continuing for fifty-three days. They found a significant growth-stimulating effect. Larger doses of the same preparation caused a growth-inhibiting effect.

McCullagh and McGurl [657] conclude in regard to epiphysial closure that an increase in the rate of epiphysial maturity beyond normal should serve as a warning to those who are inclined to give large doses of testosterone propionate to immature persons. They emphasize strongly that dwarfing might be caused by such doses being given to patients who have not attained normal adult stature.

The Source of Creatine.—Borsook and Dubnoff [658] claim a specific sensitive analytic method for the study of the precursors of creatine in animals. They use a soil bacterium which specifically destroys creatine and creatinine. They have found that slices of the liver of the cat, the rabbit and the rat are able to convert glycocyamine to creatine. In their experiments they have observed an increase of from five to twenty times the amount of creatine originally present in the slices of liver. This conversion requires methylation by the liver tissue. If methionine is added, the amount of creatine formed is 50 per cent greater on the average than if methionine is not added. Methionine is the only substance yet found by the authors among a large number of amino acids, methylated amines and other compounds which is able to effect this increase in methylation in the liver of the rat. Other animals and other substances are now being studied.

Borsook and Dubnoff [659] follow up their previous paper with an experimental study. In this, experiments showed "that glycocyamine can be methylated by the liver of every animal examined. The stimulating effect of methionine observed with rat liver was found with some but not with all the other animals. The kidney appears to be unimportant (except in the pigeon) for the methylation of glycocyamine with or without methionine." These findings are interpreted as indicating that creatine normally is formed by the methylation of glycocyamine in the liver.

Retention and Utilization of Calcium.—Pierce, Daggs, Meservi and Simcox [660] present the results of their investigation to determine the

657. McCullagh, E. P., and McGurl, F. J.: Effects of Testosterone Propionate on Epiphyseal Closure, Sodium and Chloride Balance and on Sperm Counts, Endocrinology **26**:377-384 (March) 1940.

658. Borsook, H., and Dubnoff, J. W.: Formation of Creatine from Glycocyamine in Liver, J. Biol. Chem. **132**:559-574 (Feb.) 1940.

659. Borsook, H., and Dubnoff, J. W.: Creatine Formation in Liver and in Kidney, J. Biol. Chem. **134**:635-639 (July) 1940.

660. Pierce, H. B.; Daggs, R. G.; Meservi, A. B., and Simcox, W. J.: Retention of Calcium and Phosphorus by Pre-School Children, J. Nutrition **19**:401-414 (April) 1940.

relative availability of calcium and phosphorus in milk and in so-called fortified food. The fortified food consisted of cereal to which a mixture of calcium, sodium and iron phosphates had been added. The subjects were 4 girls and 6 boys from 3 to 6 years of age. The calcium level of each subject was brought to saturation. The subjects were then divided into two groups of 2 girls and 3 boys each. The periods of diet were reversed in each group to rule out weather or seasonal effects. They were maintained on carefully regulated basal diets.

The authors conclude that there is no appreciable difference of retention of calcium and phosphorus with the use of the different salts; utilization of calcium and phosphorus was equally good with milk and with fortified cereal. The daily storage of calcium was 11 to 12 mg. per kilogram of body weight; the daily storage of phosphorus was 7 to 8 mg. per kilogram of body weight. About 19 per cent of the calcium and 11 per cent of the phosphorus were retained. To obtain maximal retention of calcium it was necessary to give over 700 mg. daily.

Kempster and associates [661] state that previous experiments have shown that only about one fifth of the calcium ingested in milk is utilized. Experiments were made to determine the utilization of the calcium of dicalcium phosphate. Six small boys served as subjects. They were fed two levels of calcium. It was found that the utilization of calcium of dicalcium phosphate by these subjects averaged 19.5 per cent. Hence the authors conclude that there is no superiority of dicalcium phosphate over milk as a source of calcium.

Arthrography.—Tarafa [662] concludes that the injection of a contrast medium into the joints is indicated in cases in which one wishes to examine the soft parts within the joint, such as a meniscus, the capsule or a cruciate ligament, or some foreign body, tumor or other intra-articular change. Penetration of air between the plate and the meniscus of the tibia is seen in the arthropneumoroentgenogram when detachment of the meniscus is present. Tear of the meniscus appears as a more or less irregular interruption at the site of the rupture. Tearing off of the cruciate ligaments produces some change in the normal picture, often associated with fracture of the spine of the tibia. With arthritis an enlargement of the capsule and irregularities in its walls are observed. An intra-articular tumor shows a perfectly defined outline while an extra-articular tumor squeezes and displaces the capsule. Loose bodies in the joint appear well defined. With Charcot's knee joint,

661. Kempster, E., and others: Utilization of Calcium of Dicalcium Phosphate by Children, J. Nutrition **20**:279-287 (Sept.) 1940.

662. Tarafa, J. I.: Arthropneumoradiography, Cir. ortop. y traumatol., Habana **8**:3-17 (Jan.-March) 1940.

besides a marked increase of the joint space and abnormal features of the joint surface, an almost complete destruction of the soft parts is evident.

Paas [663] describes a method of visualizing the knee joint by the injection of a contrast material known as "abrodil" (skiodan N. N. R.) in a 20 per cent solution and of one known as "perabrodil" (diodrast N. N. R.) in a 35 per cent solution. Experimental work was done on dogs. The author finds that the resorption time of the material depends on both the age of the subject and the condition of the joint. With acute inflammation of the capsule of the joint the resorption is faster than normal. Active and passive motion also increase the rapidity of resorption. The tension and space of the joint depend on the position of the joint during examination. In extension the anterior part of the capsule has the least tension; in flexion the posterior part has the least tension. The normal capsular apparatus has marked elasticity. In advanced age after a long period of freedom from weight bearing, there is a shortening of the structure of the capsule with loss of elasticity. Freedom from weight bearing and advanced age diminish the ability of the capsule to resorb the contrast materials.

The Dynamics of Muscle and Bone.—Heppel [664] presents the results of his study of the changes that take place in muscles when stimulated, especially changes in potassium, sodium chloride and water, as related to the age of the animal. All of the work was done on young rats at the age of 5 to 6 weeks. The changes observed in these animals are twice as great as in older rats. Heppel also studied the influence of diet, tension, duration of stimulation and poisoning with monoiodoacetic acid on the electrolyte changes.

His conclusions are as follows:

1. The loss of potassium on stimulation of rat muscles is progressively greater as the duration of contraction is increased. After 30 minutes there is no further change, at least for another half-hour.

2. The changes in chloride and water are almost maximal after 5 minutes of stimulation; after 1 hour the changes are very much reduced in magnitude.

3. The individual variations in the water changes follow closely those of chloride, but there is no correlation with the variations in the potassium changes. The potassium loss and the chloride gain apparently bear a different relationship to the contraction processes.

4. Previous work relating to the changes during recovery is confirmed.

5. Young rats of about 6 weeks of age are able to lose more potassium from their muscles on stimulation than is the case for adult rats.

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663. Paas, H. R.: Study of Capsule by Means of Positive Contrast Fluid and Fluoroscopy, Deutsche Ztschr. f. Chir. **252**:478-498, 1939.

664. Heppel, L. A.: Effect of Age and Diet on Electrolyte Changes in Rat Muscle During Stimulation, Am. J. Physiol. **128**:440-448 (Feb.) 1940.

6. Feeding diets low in potassium and poisoning with monoiodoacetic acid have little or no effect on the potassium changes during stimulation. Previous work on the influence of tension is confirmed.

Elftman [665] has previously described a method for determining the muscle forces and their activity as applied to walking. Now he describes the same method as applied to running.[666] The determinations were made by analysis of photographic films. The moments of force resulting from the muscles acting about the joints of the limbs and the rates at which they do work were determined for a running step. The energy requirement arrived at in this way represents a minimum for the step concerned; it does not include energy used for the maintenance of tension in muscles which are not changing in length or for the duplication involved in the simultaneous action of antagonists.

The muscles of the limb did work at the rate of 2.61 horsepower. If all the muscles of the body were included and no energy was lost through friction, the rate would be at least 2.89 horsepower.

Work done by the muscles of the limb was divided as follows: against wind resistance, 0.15 horsepower; fluctuations in the total energy of the body, 1.37 horsepower; distribution of energy between the parts of the body, 1.09 horsepower. If one joint muscles were present, additional work at the rate of 1.36 horsepower would be necessary. The saving of this amount by two joint muscles illustrates the importance of the disposition of muscles in determining muscular work.

Miller and Darrow [667] present some experimental work which attempts to throw some light on whether changes in the electrolyte pattern within the muscle cell affect the ability of the cell to perform work. Other investigators have shown that muscle activity may be affected by rapid changes in extracellular electrolyte. The experimental procedure used by the authors altered the potassium of skeletal muscle, and they studied the response of the muscle to repeated tetanic stimulation. They conclude that there is no direct relation between the amount of potassium in the muscle or serum and the type of response to the tetanic stimulation obtained. It is felt that this lack of correlation in the data is evidence against the belief that the myasthenia noted in adrenal insufficiency is due specifically to increase in the potassium of skeletal muscle.

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665. Elftman, H.: Forces and Energy Changes in the Leg During Walking, Am. J. Physiol. **125**:339-356 (Feb.) 1939; Function of Muscles in Locomotion, ibid. **125**:357-366 (Feb.) 1939.

666. Elftman, H.: Work Done by Muscles in Running, Am. J. Physiol. **129**: 672-684 (June) 1940.

667. Miller, H. D., and Darrow, D. C.: Effect of Changes in Muscle Electrolyte on Response of Skeletal Muscle to Tetanic Stimulation with Particular Reference to Potassium, Am. J. Physiol. **129**:264-270 (May) 1940.

Milch [668] presents the results of his studies of the relation of the contour of bone to forces exerted on bone. His studies were made by subjecting bone models made with polymerized phenylformaldehyde resins to stress. When such resins are subjected to stress they realine themselves to fit the molecular structure to which they have been applied, depending on the changes of the lines of stress. Such lines of stress can be visualized under polarized light and then photographed. The author studied models of normal bone and bone which had been alined by osteotomies. He also studied an os calcis and a whole foot.

When the outline of the normal femur was compressed, several interesting phenomena were observed. The arrangement of the lines of stress was found to be reminiscent of the trabecular structure seen on longitudinal section of the femur. When the model was shifted first to one side and then the other to simulate abduction and adduction under weight bearing, these stress lines shifted so that they resembled first one and then the other of the longitudinal trabecular systems. The stress lines seemed to run between the two points of compression and apparently did not radiate into the trochanteric region to any noticeable extent. The greater number of stress lines appeared to be on the medial side of the shaft, toward the line of the mechanical axis of the normal femur. The stress lines seemed to stop in an area which was situated close to the normal epiphysial zone. This stress pattern was repeatedly reproduced. It could be modified by adding the element of traction to that of compression.

The author suggests that this method of analysis could be applied to a great variety of clinical and theoretic problems for study, and eventually a fuller knowledge of the predetermined lines of stress when planning realinements of the extremities would be gained.

668. Milch, H.: Photo-Elastic Studies of Bone Forms, J. Bone & Joint Surg. **22**:621-626 (July) 1940.